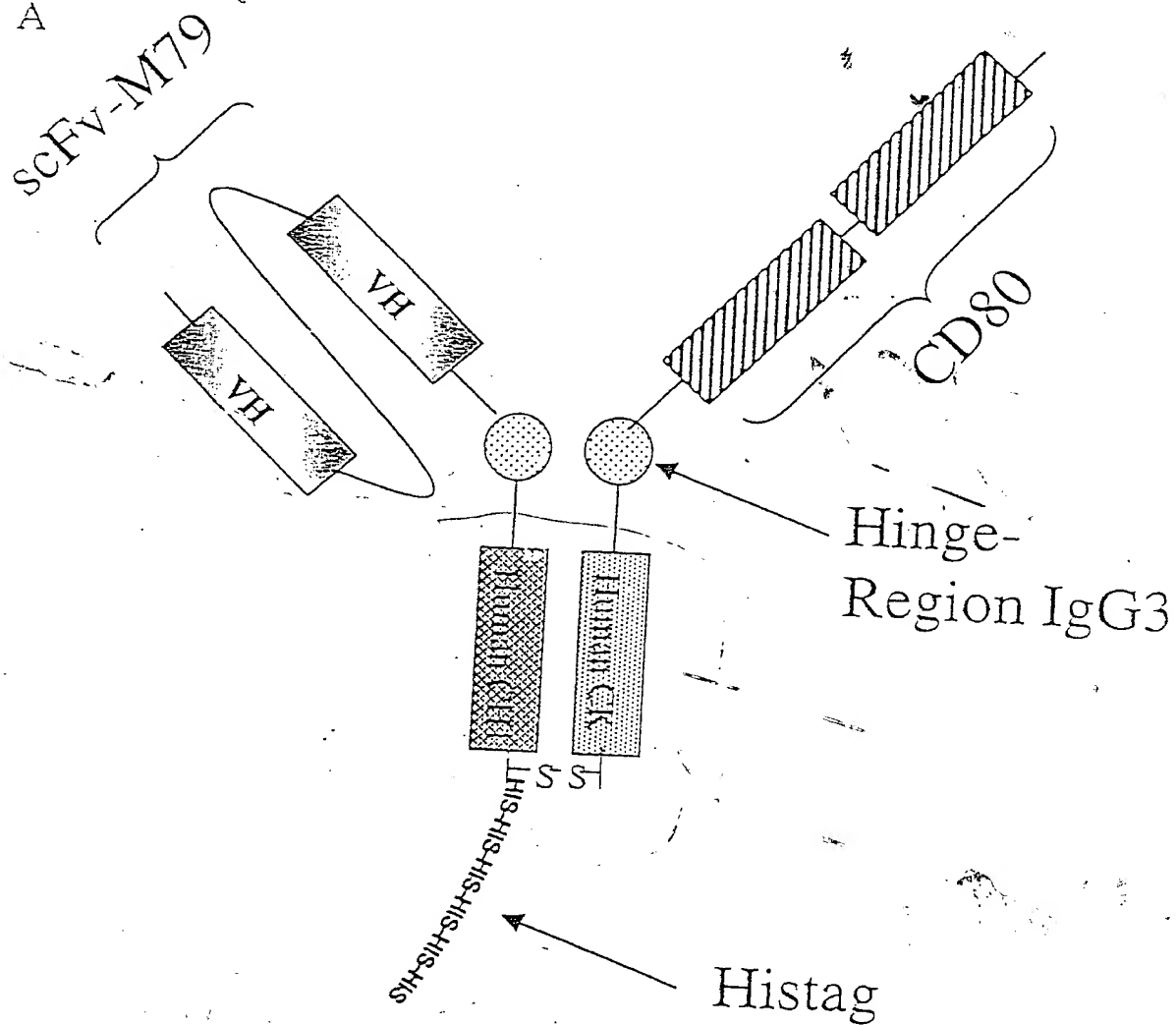
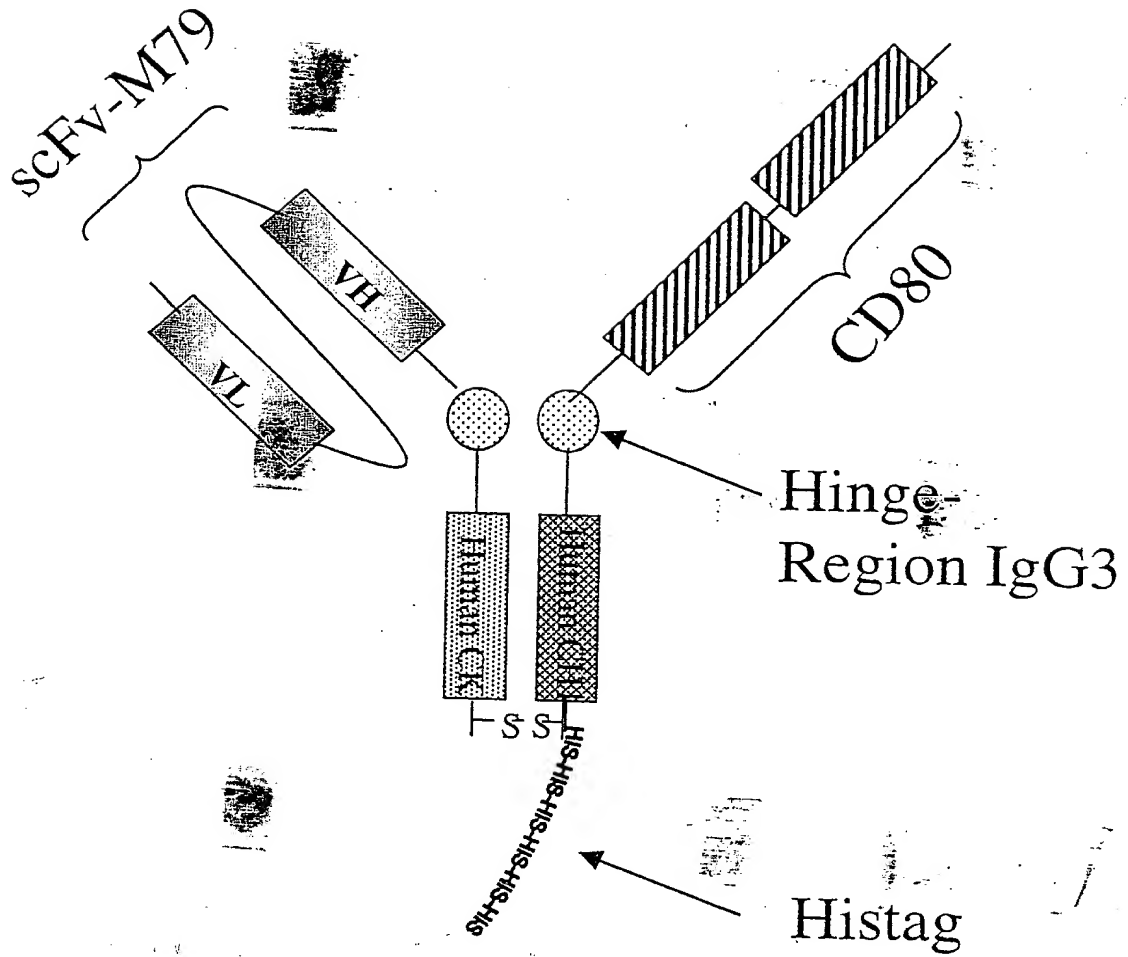
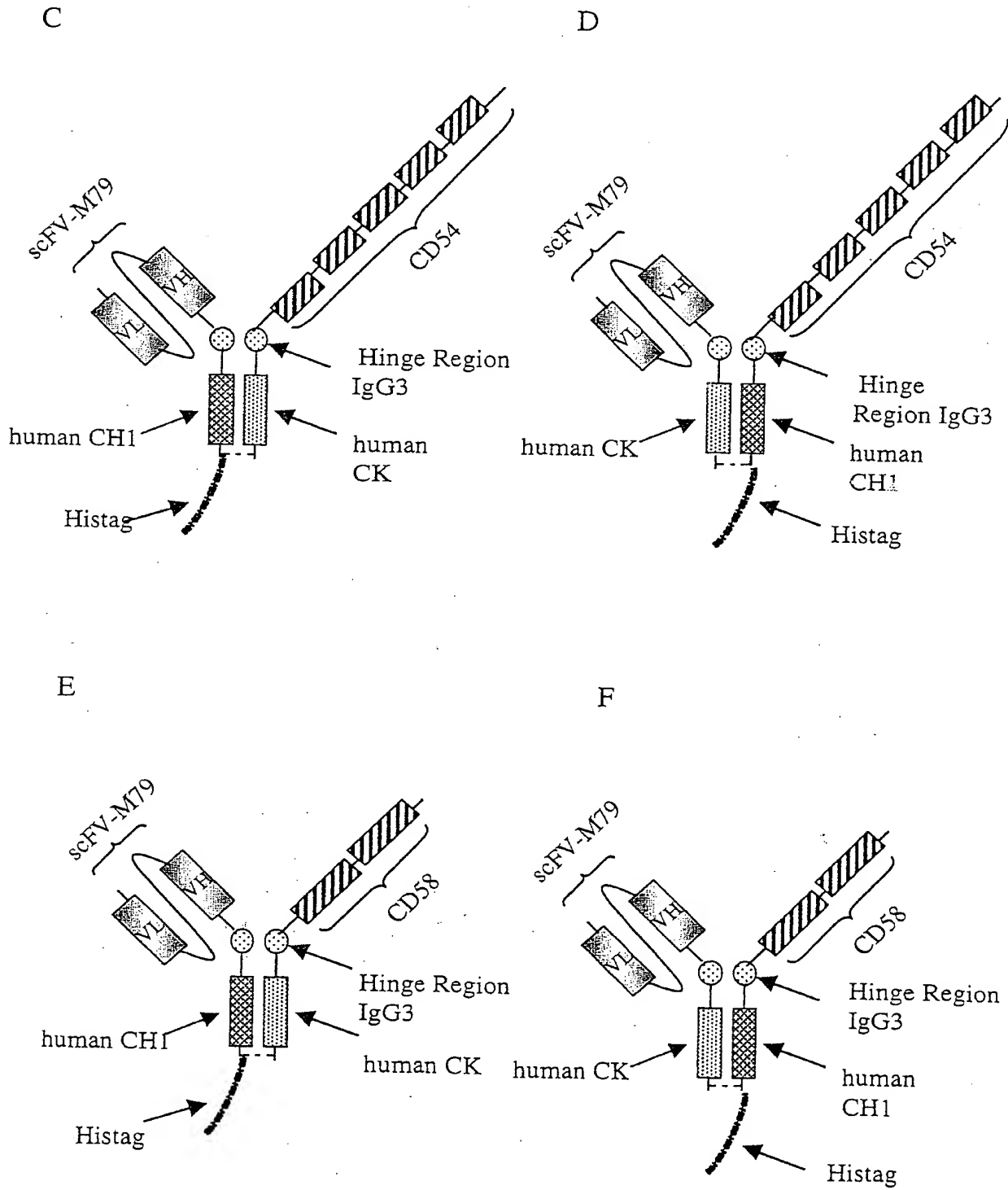


A



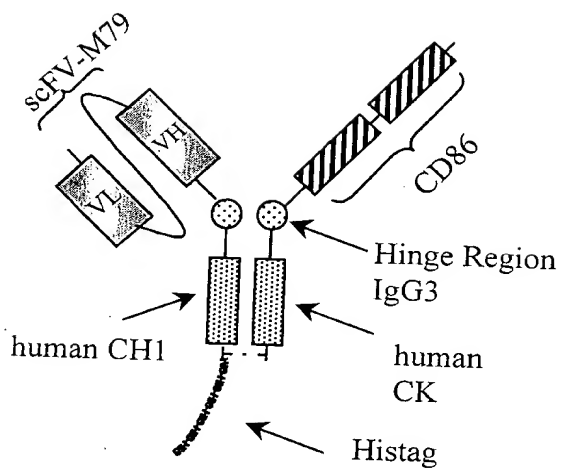
B



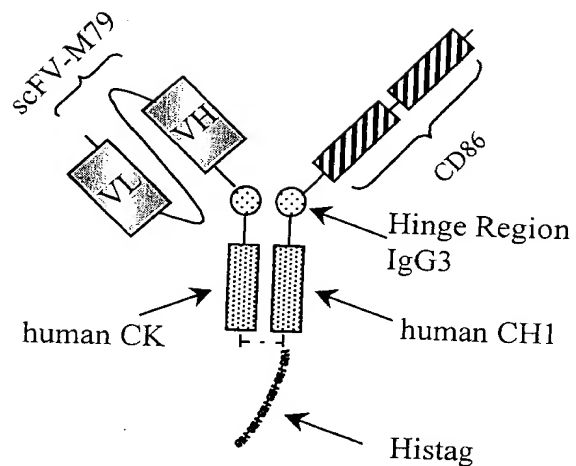


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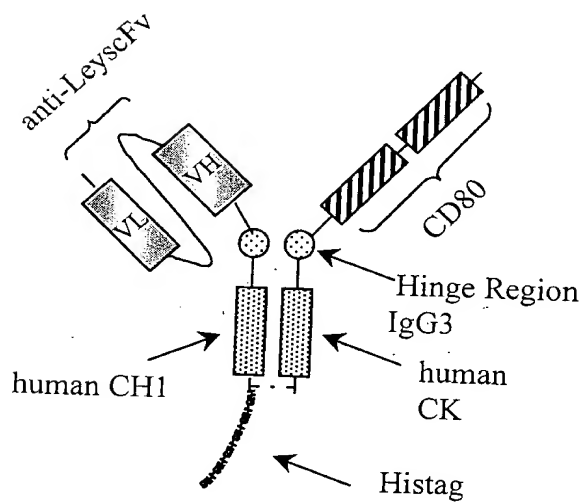
G



H



I



J

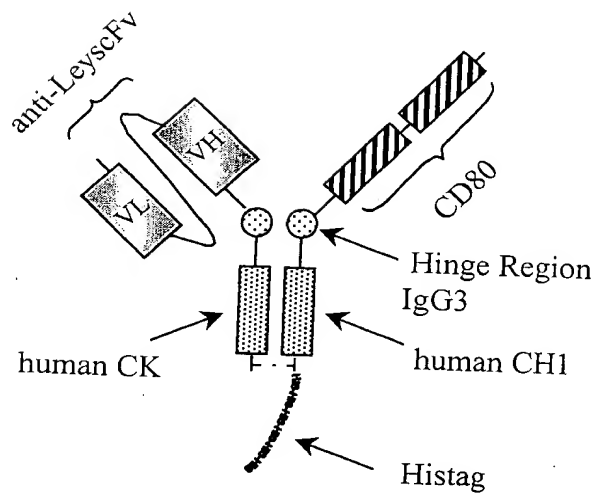
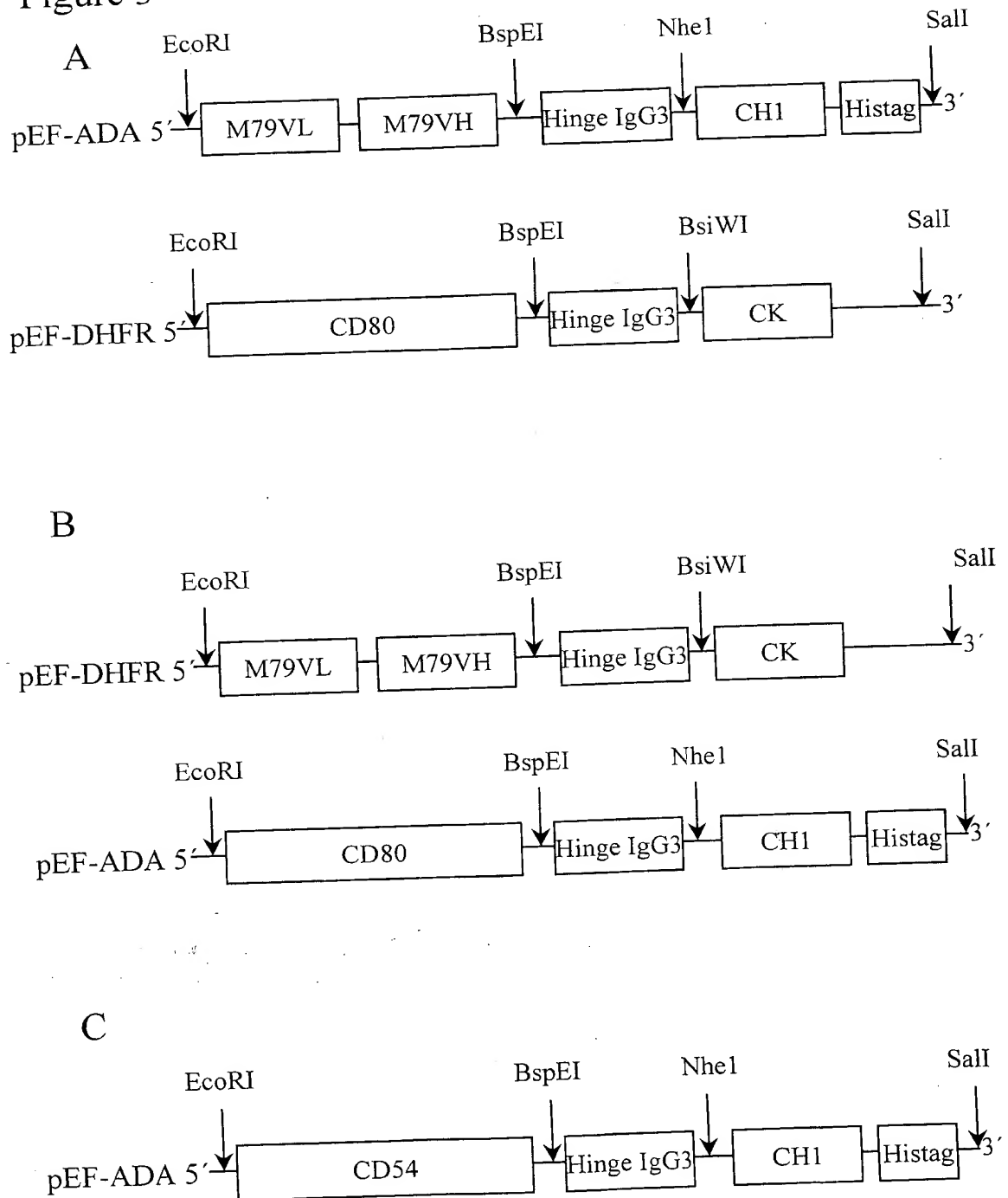


Figure 2

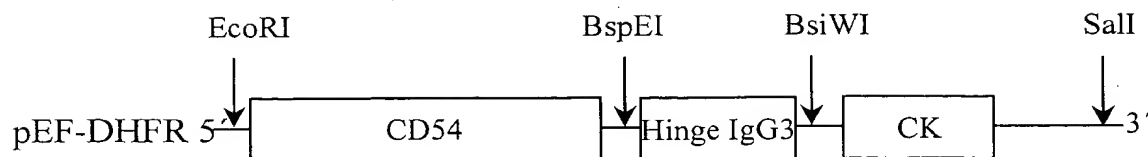
EcoRI
XbaI *AsuII* *BspEI* *BamHI* *EcoRV* *XmaI*
5' CTA GAA TTC TTC GAA TCC GGA GGT GGT GGA TCC GAT ATC CCC GGG
SalI
CAT CAT CAC CAT CAT CAT TGA G 3'

09/744625-074604

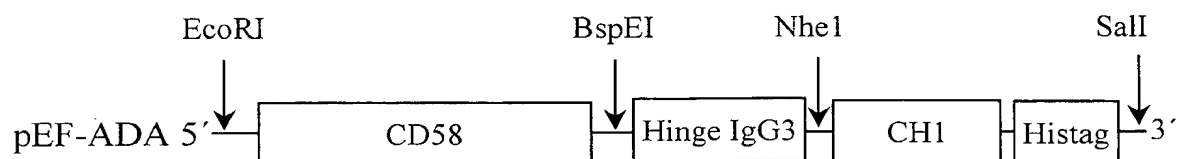
Figure 3



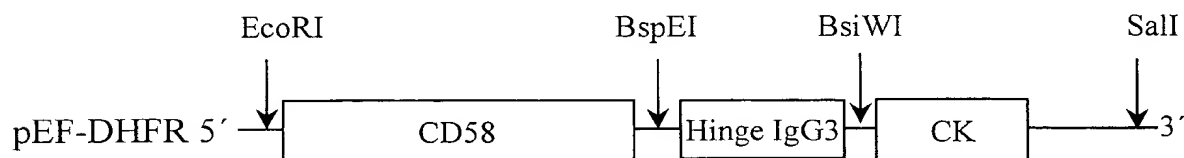
D



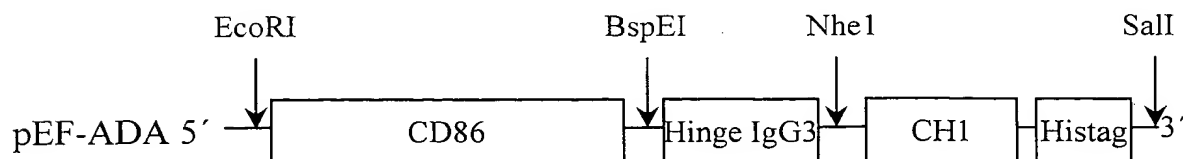
E



F

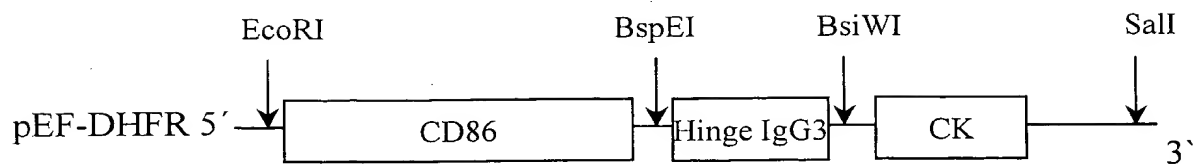


G

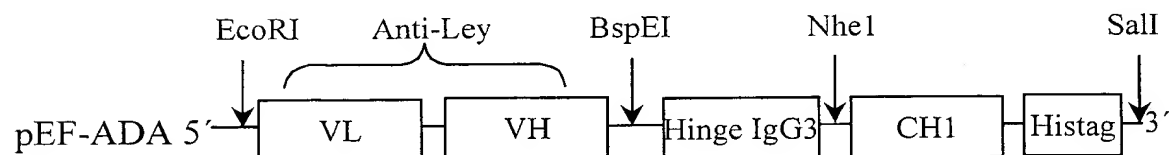


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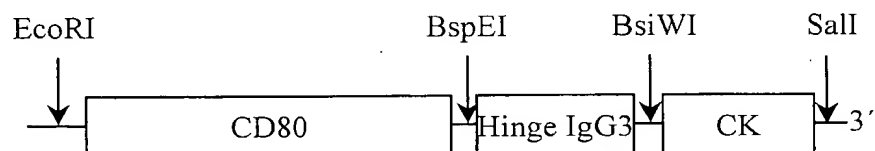
H



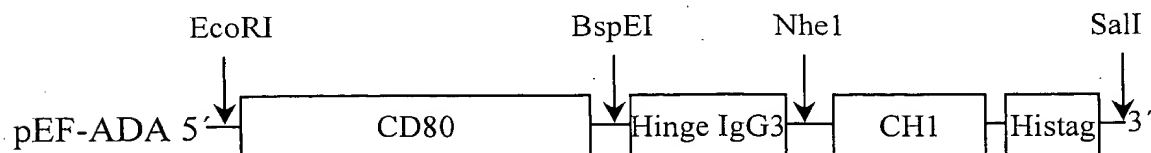
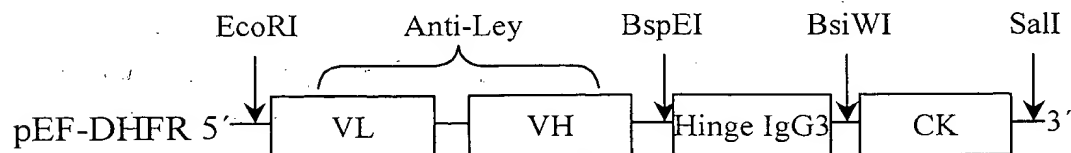
I



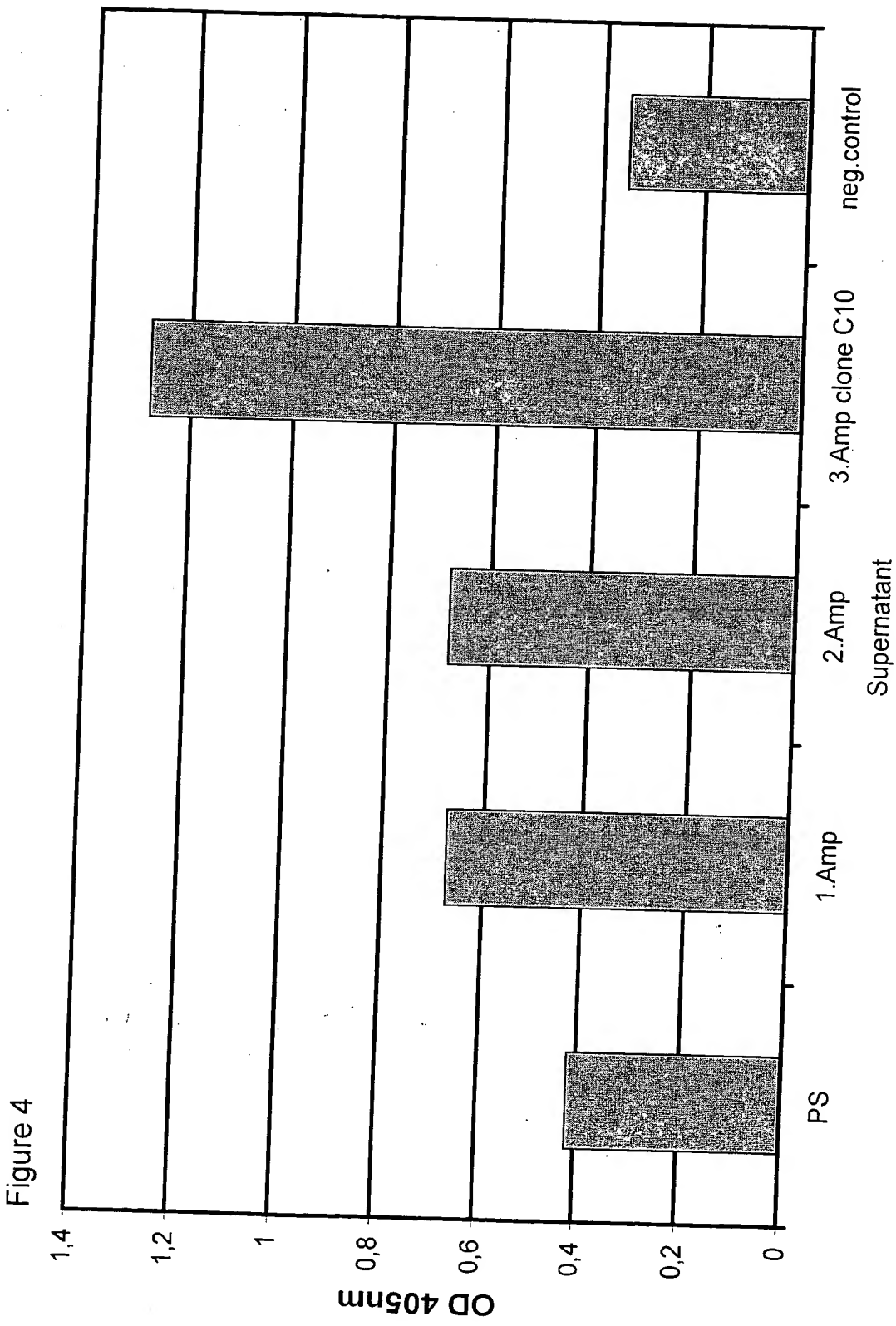
pEF-DHFR 5'



J



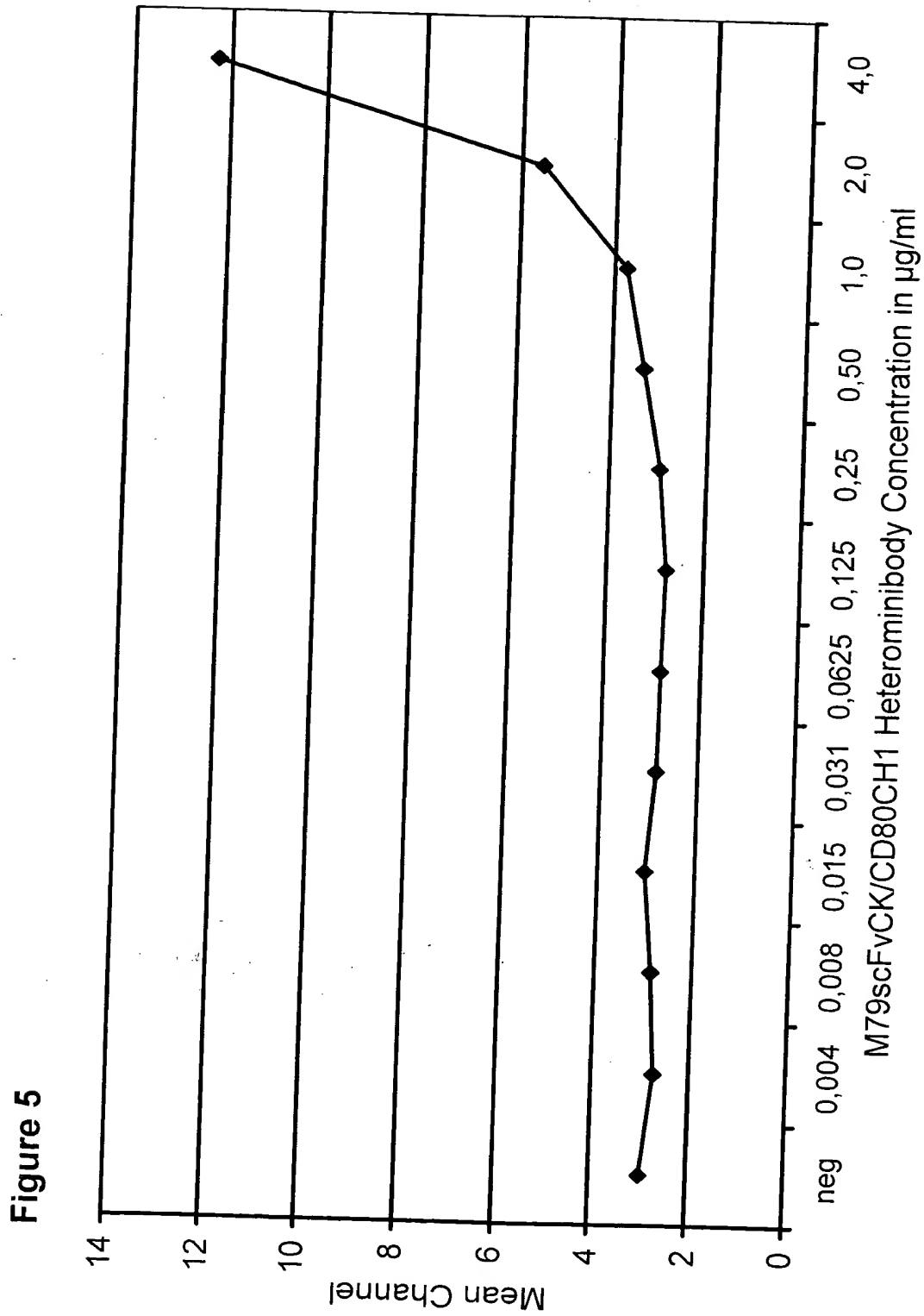
9/75



1008 000 000

105420-5234460

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Figure 6

EcoRI		10	19			28			37			46			55		
5'	GAAT TCC	ACC	ATG	GGA	TGG	AGC	TGT	ATC	ATC	CTC	TTC	TTG	GTA	GCA	ACA	GCT	ACA
			---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
			M	G	W	S	C	I	I	L	F	L	V	A	T	A	T
		64	73			82			91			100			109		
	GGT GTA CAC	TCC	GAT	ATC	GTT	GTG	ACT	CAG	GAA	TCT	GCA	CTC	ACC	ACA	TCA	CCT	
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	G	V	H	S	D	I	V	V	T	Q	E	S	A	L	T	T	S
		118	127			136			145			154			163		
	GGT GAA ACA	GTC	ACA	CTC	ACT	TGT	CGC	TCA	AGT	ACT	GGG	GCT	GTT	ACA	ACT	AGT	
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	G	E	T	V	T	L	T	C	R	S	S	T	G	A	V	T	S
		172	181			190			199			208			217		
	AAC TAT GCC	AAC	TGG	GTC	CAA	GAA	AAA	CCA	GAT	CAT	TTA	TTC	ACT	GGT	CTA	ATA	
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	N	Y	A	N	W	V	Q	E	K	P	D	H	L	F	T	G	I
		226	235			244			253			262			271		
	GGT GGT ACC	AAC	AAC	CGA	GTT	CCA	GGT	GTT	CCT	GCC	AGA	TTC	TCA	GGC	TCC	CTG	
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	G	G	T	N	N	R	V	P	G	V	P	A	R	F	S	G	L
		280	289			298			307			316			325		
	ATT GGA GAC	AAG	GCT	GCC	CTC	ACC	ATC	ACA	GGG	GCA	CAG	ACT	GAG	GAT	GAG	GCA	
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	I	G	D	K	A	A	L	T	I	T	G	A	Q	T	E	D	A
		334	343			352			361			370			379		
	ATA TAT TTC	TGT	GCT	CTA	TGG	TAC	AGC	AAC	CAT	TGG	GTG	TTC	GGT	GGA	GGA	ACC	
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	I	Y	F	C	A	L	W	Y	S	N	H	W	V	F	G	G	T
		388	397			406			415			424			433		
	AAA CTC GAG	GTC	CTA	GGT	GGT	GGT	GGT	TCT	GGC	GGC	GGC	GGC	TCC	GGT	GGT	GGT	
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	K	L	E	V	L	G	G	G	G	S	G	G	G	G	S	G	G
		442	451			460			469			478			487		
	GGT TCT CAG	GTC	CAG	CTG	CAG	GAG	TCT	GGA	CCT	GGC	CTG	GTG	GCG	CCC	TCA	CAG	
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	G	S	Q	V	Q	L	Q	E	S	G	P	G	L	V	A	P	Q

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496	505	514	523	532	541
AGC CTG TCC ATC ACA TGC ACC ATC TCA GGG TTC TCA TTA ACT AAG TAT GGT GTA					
S L S I T C T I S G F S L T K Y G V					
550	559	568	577	586	595
CAC TGG GTT CGC CAG CCT CCA GGA AAG GGT CTG GAG TGG CTG GTG GTG ATA TGG					
H W V R Q P P G K G L E W L V V I W					
604	613	622	631	640	649
ACT GAT GGA GGC ACA TCC TAT AAT TCA GCT CTC AAA TCC AGA CTG AGC ATC ACC					
T D G G T S Y N S A L K S R L S I S					
658	667	676	685	694	703
AAG GAC AAC TCC AAG AGC CAA GTT TTC TTA AAA ATG AAC AGT CTC CAA ACT GAT					
K D N S K S Q V F L K M N S L Q T D					
712	721	730	739	748	757
GAC ACA GCC ATG TAC TAC TGT GCC AGA CAG GAT AGA TAC GAC GGT GGA ATT GCT					
D T A M Y Y C A R Q D R Y D G G I A					
766	775	784	<u>BspEI</u>		
TAC TGG GGC CAA GGG ACC ACG GTC ACC GTC TCC TCC GGA 3'					
Y W G Q G T T V T V S S					

00744625-00150

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Figure 7

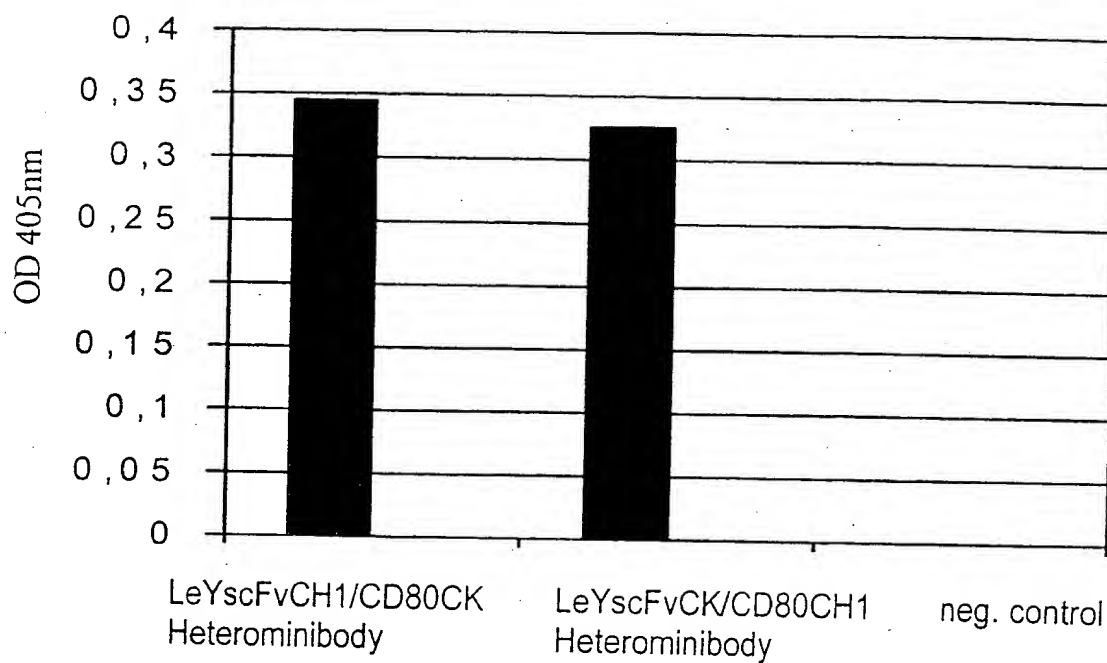
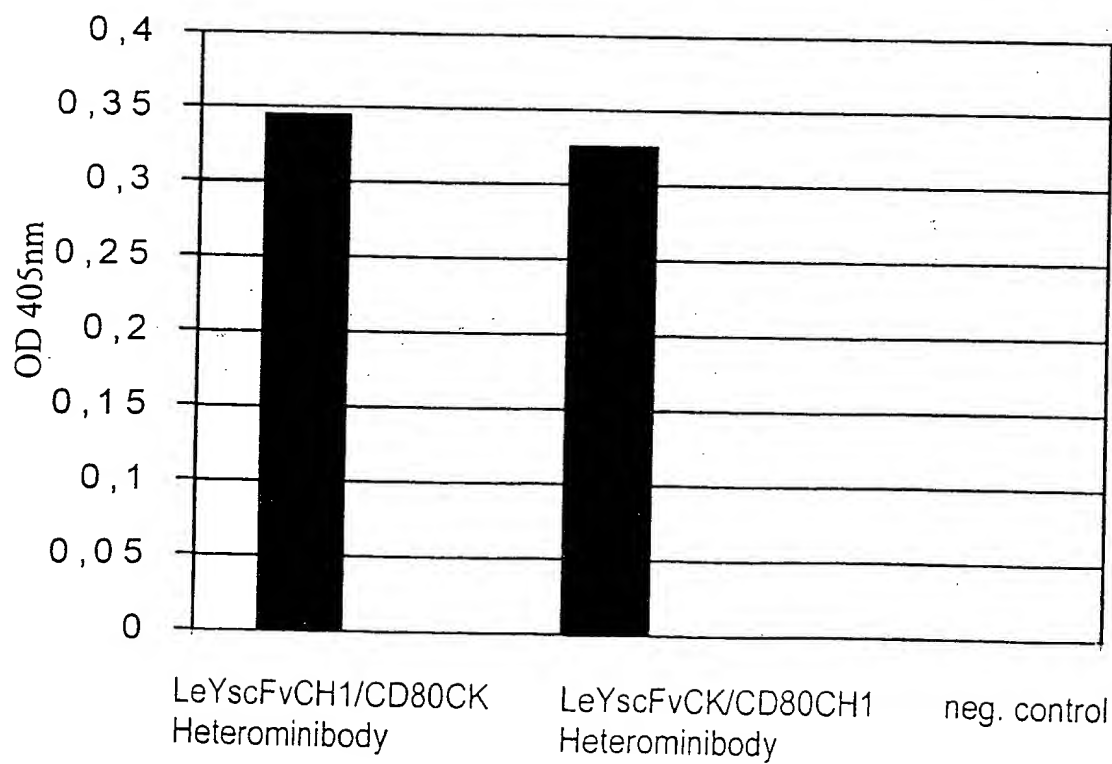
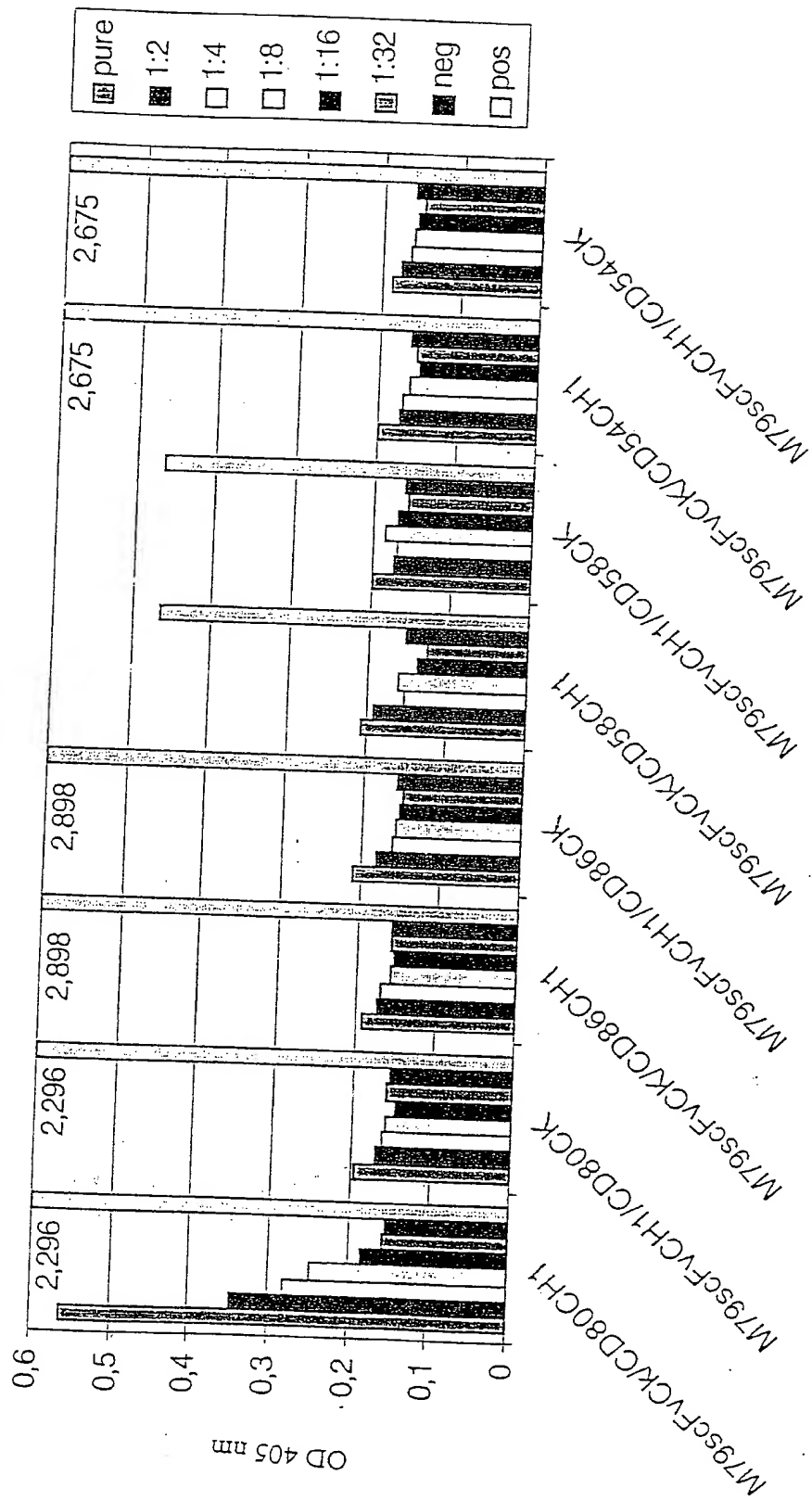


Figure 8





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Figure 10

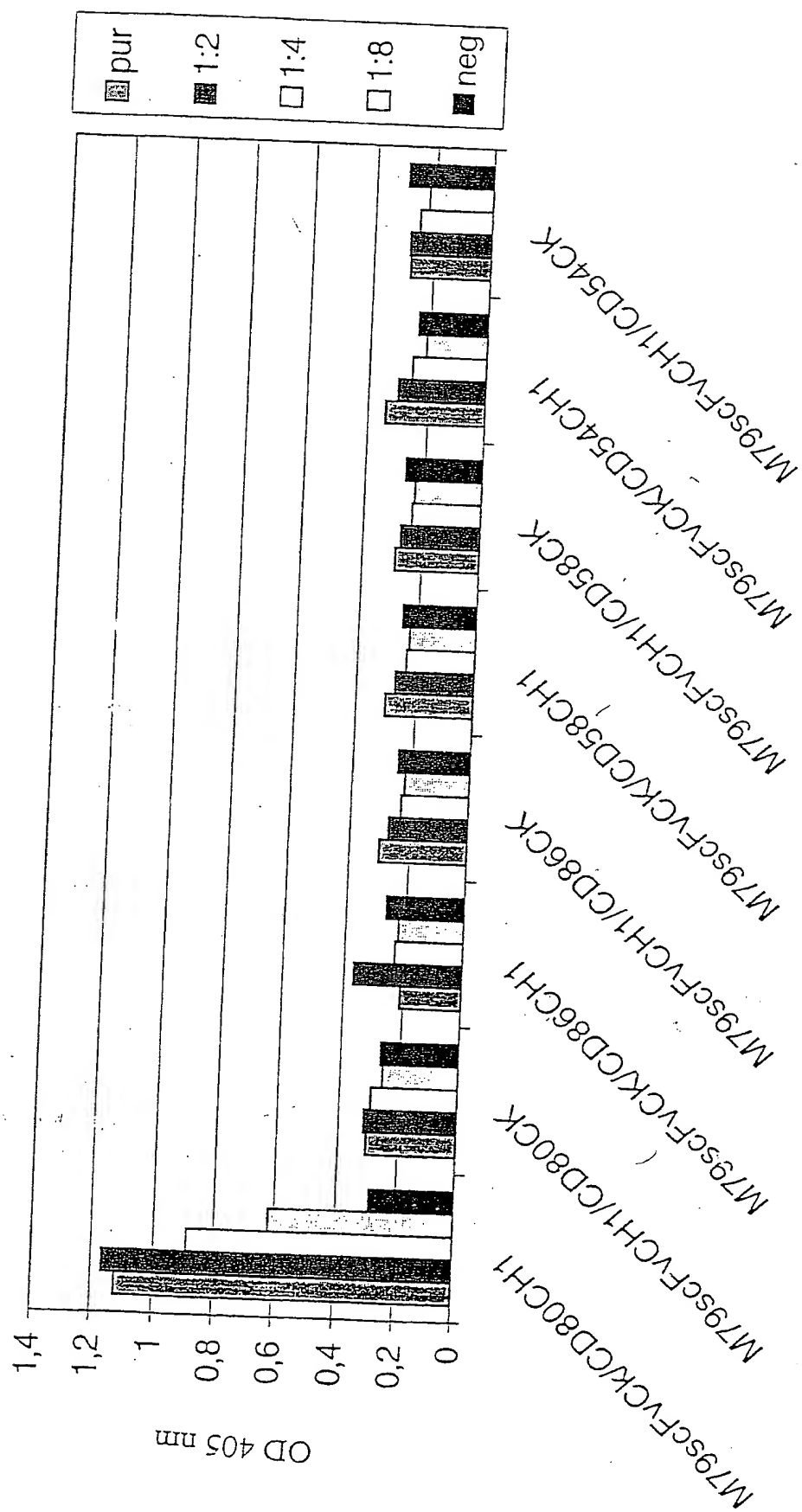
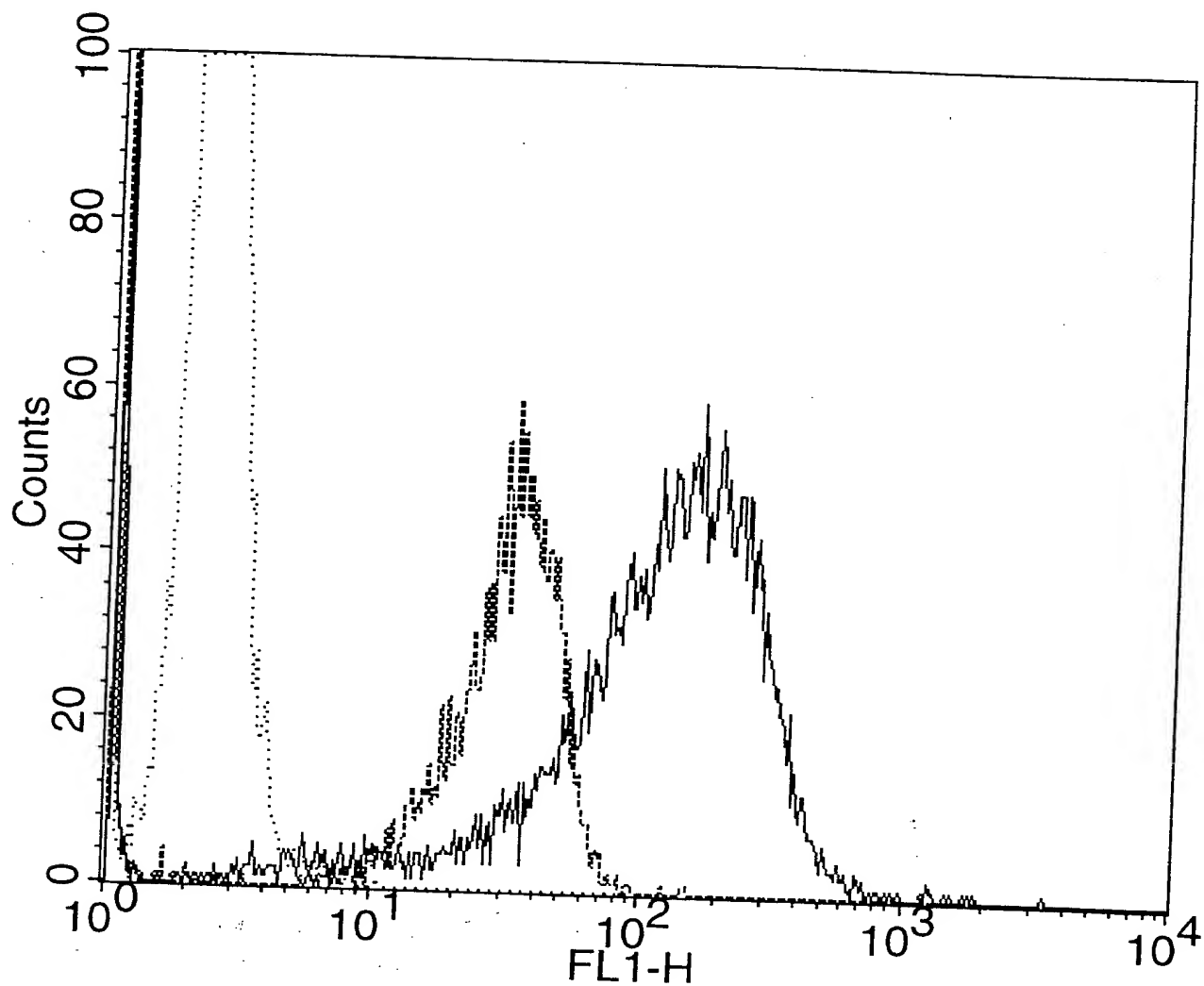
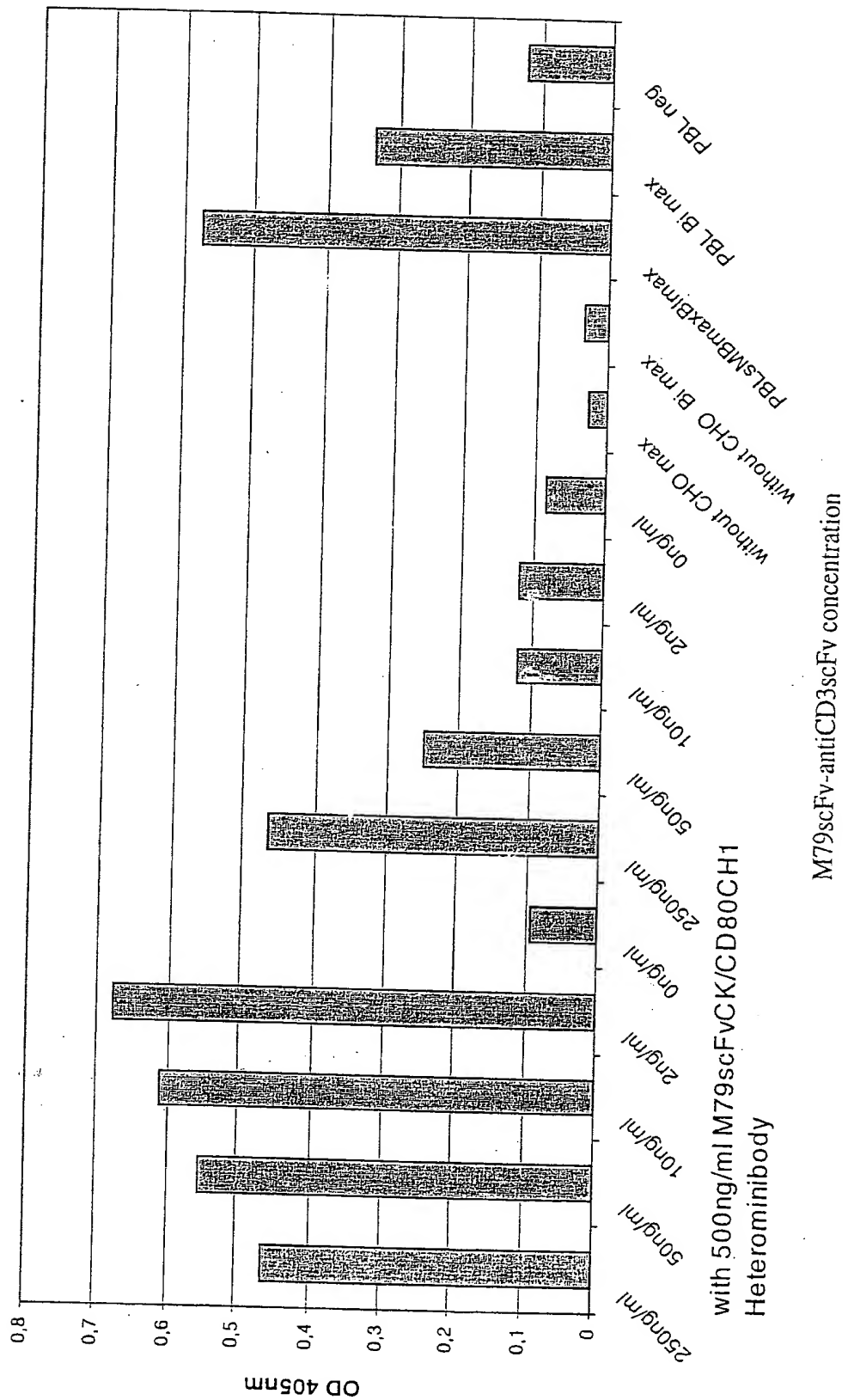


Figure 11

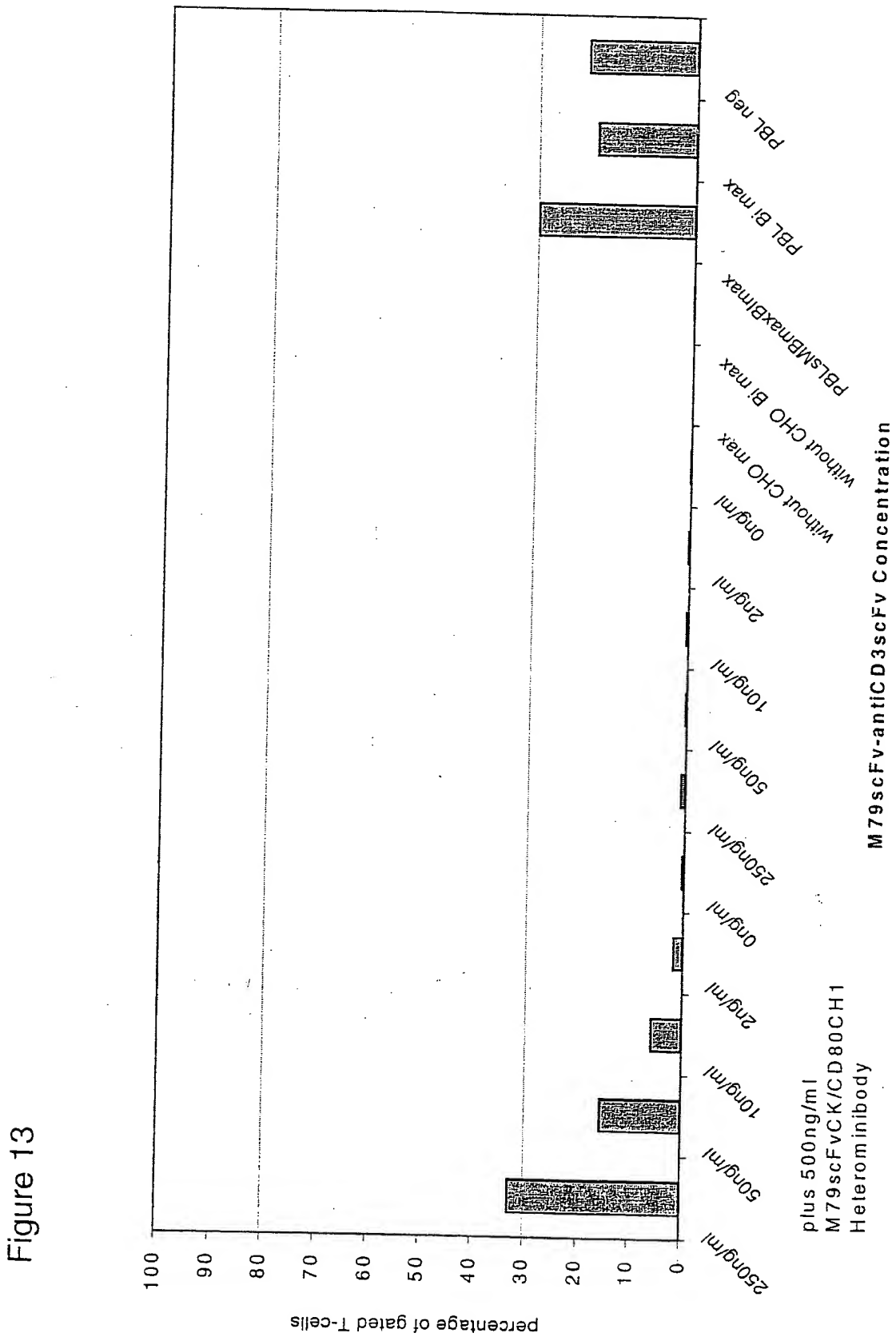


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Figure 12

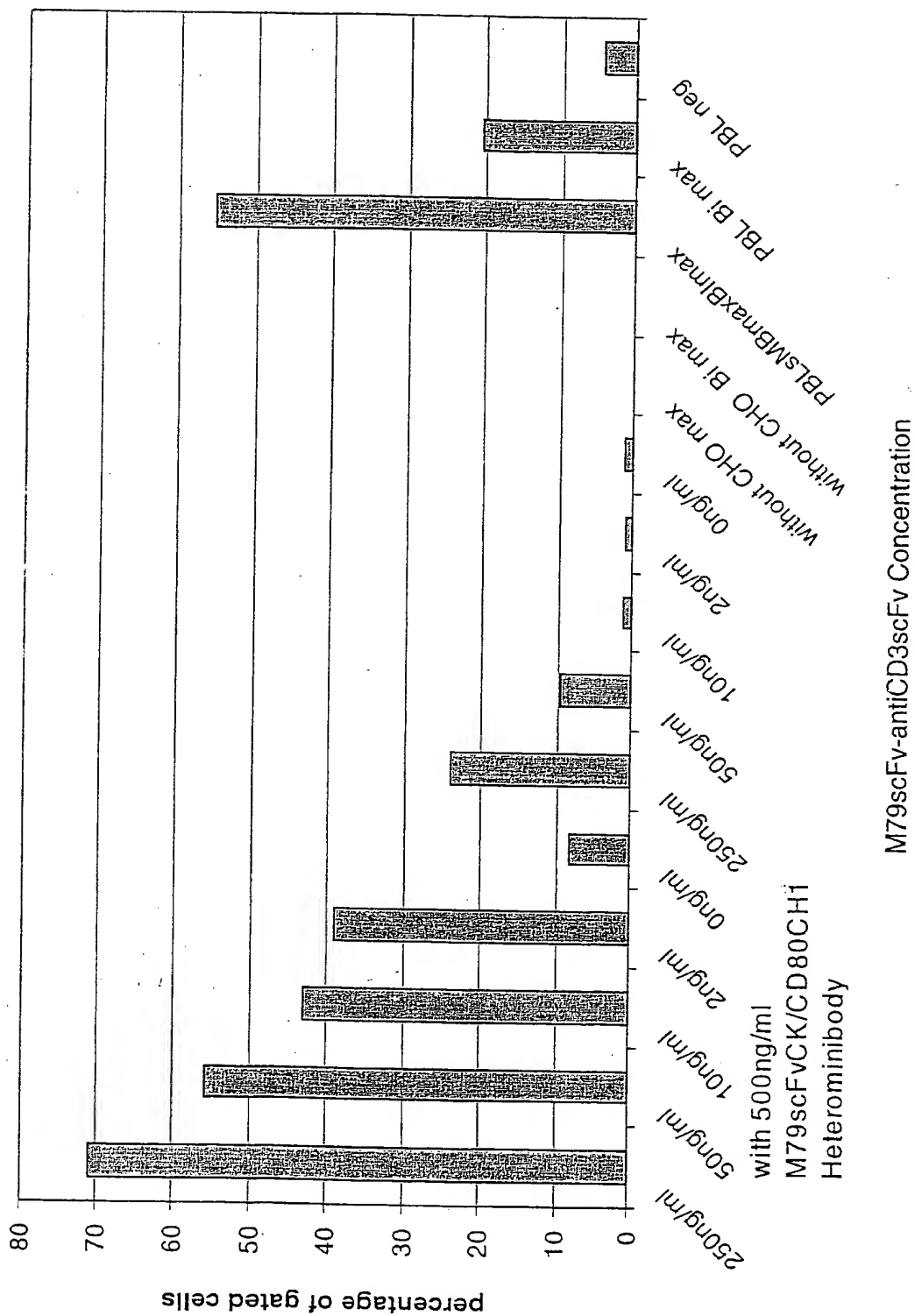


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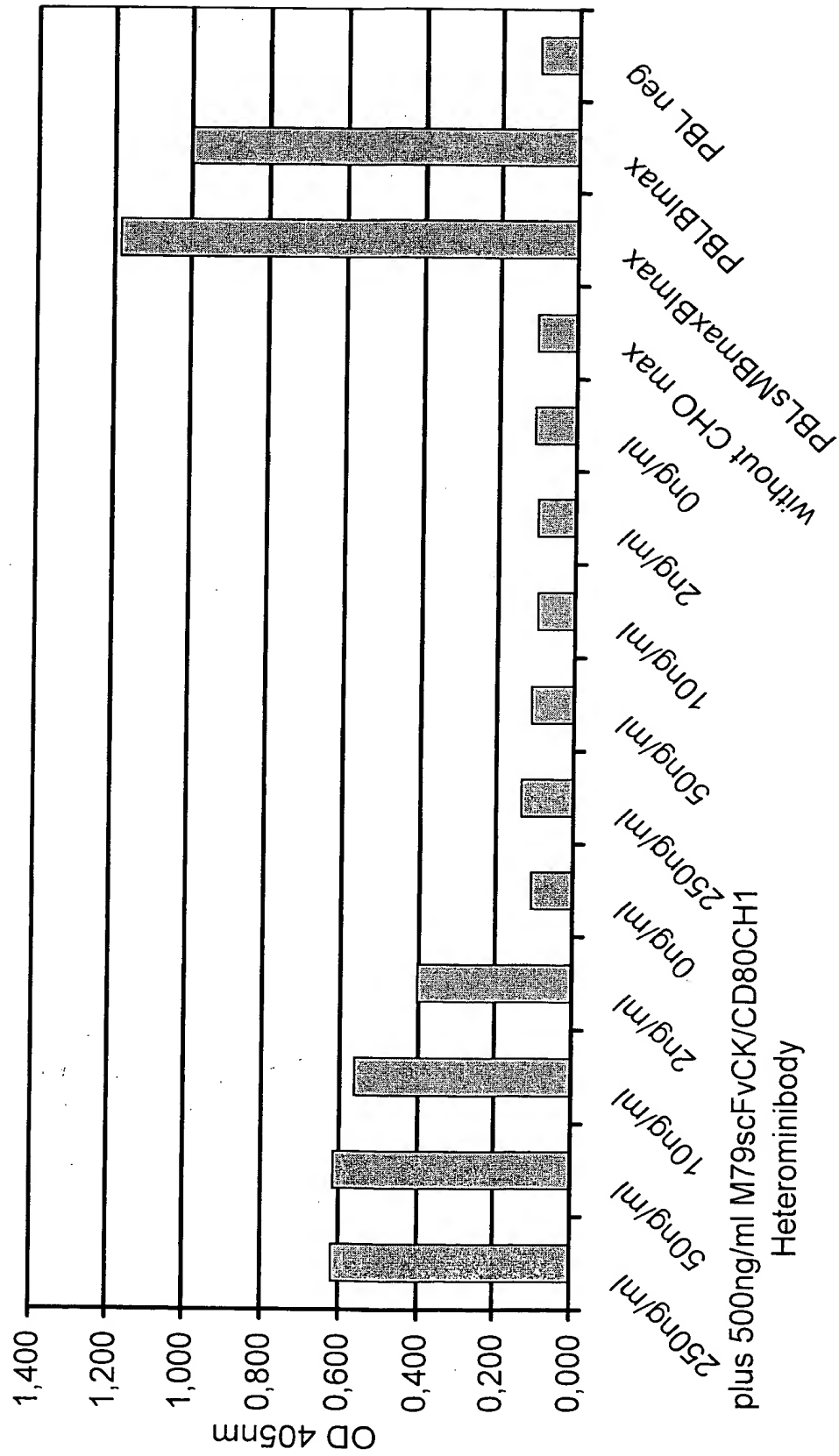
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Figure 14



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Figure 15

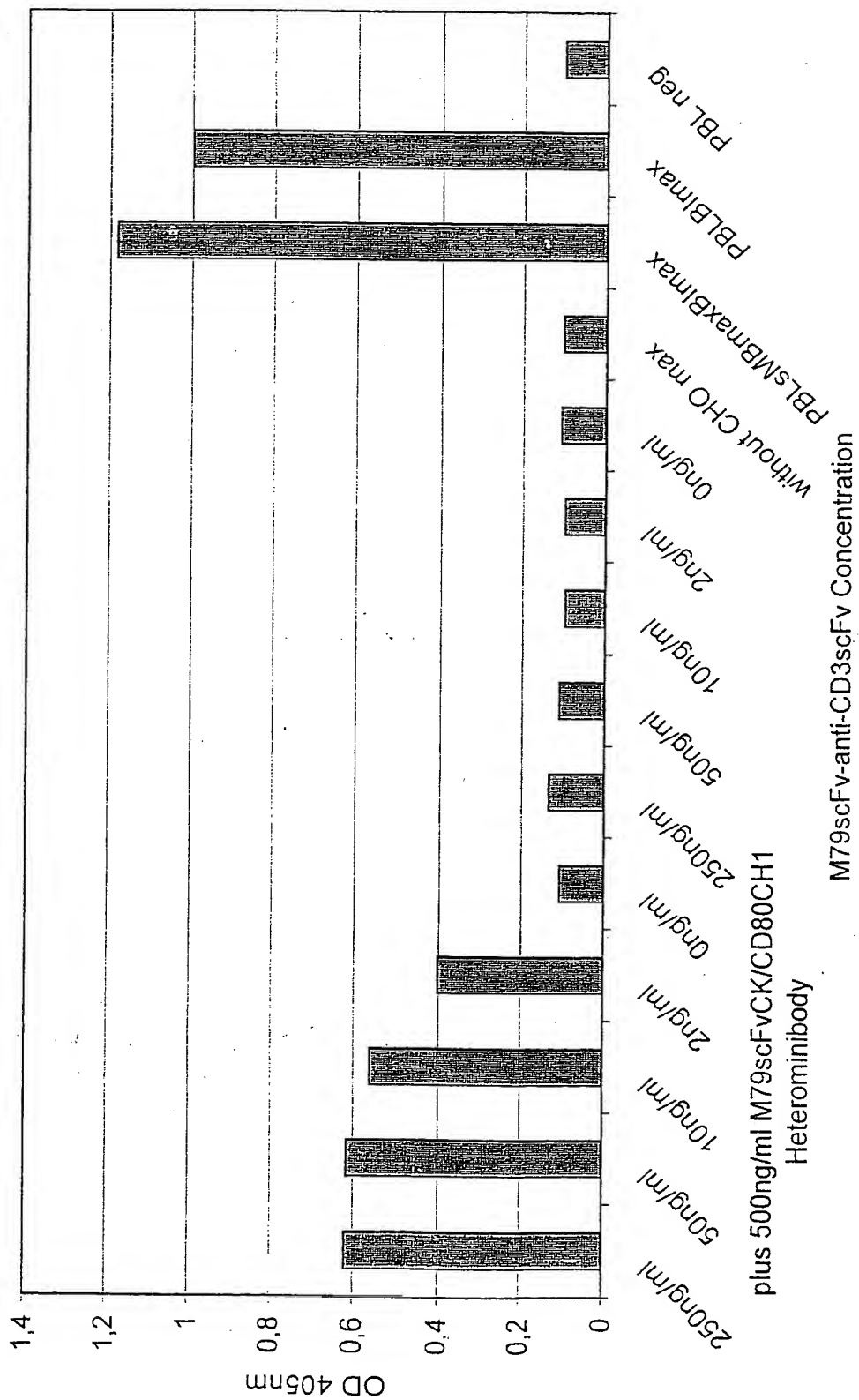


M79scFv-anti-CD3scFv Concentration

Heterominiibody

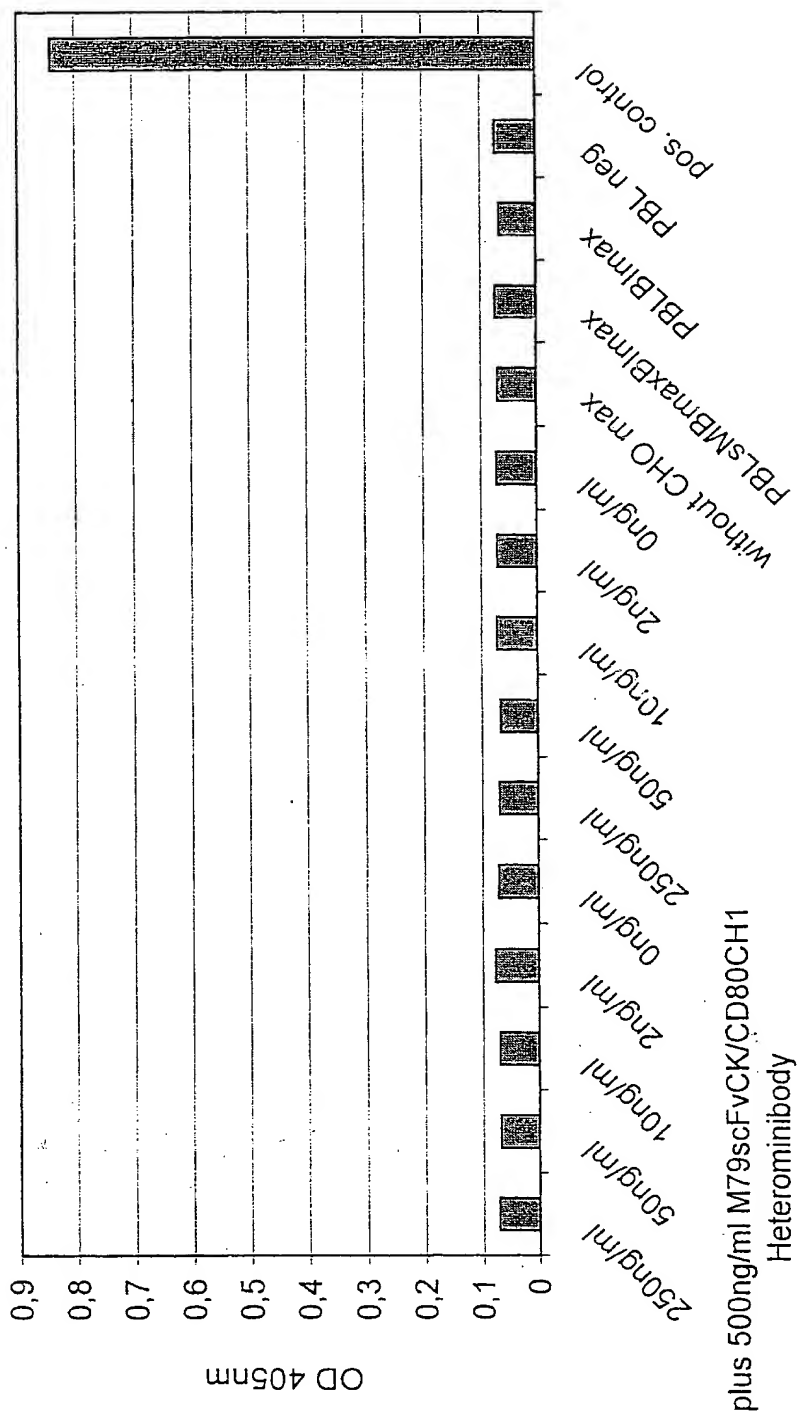
09/744625

Figure 16



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Figure17

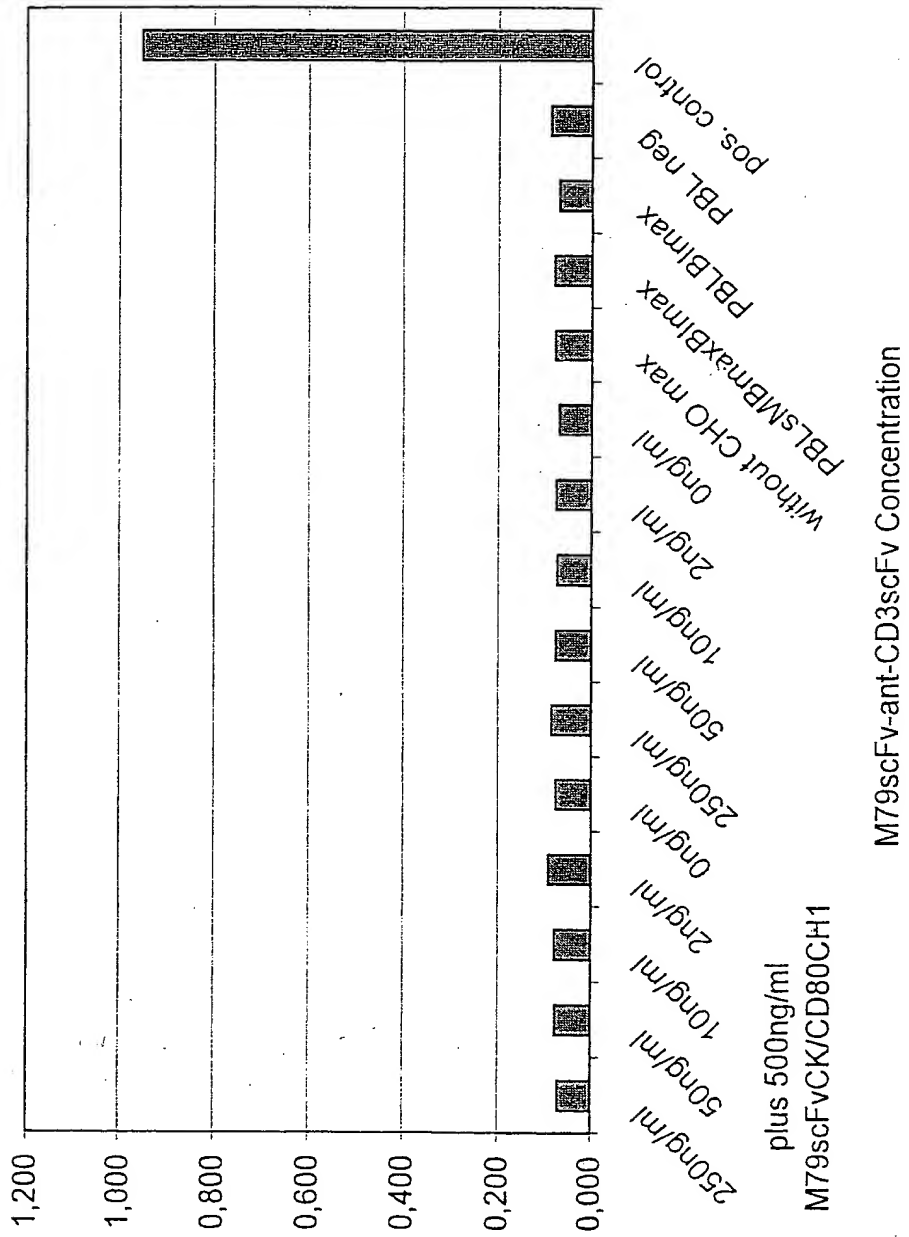


M79scFv-anti-CD3scFvConcentration

plus 500ng/ml M79scFvCK/CD80CH1
Heterominibody

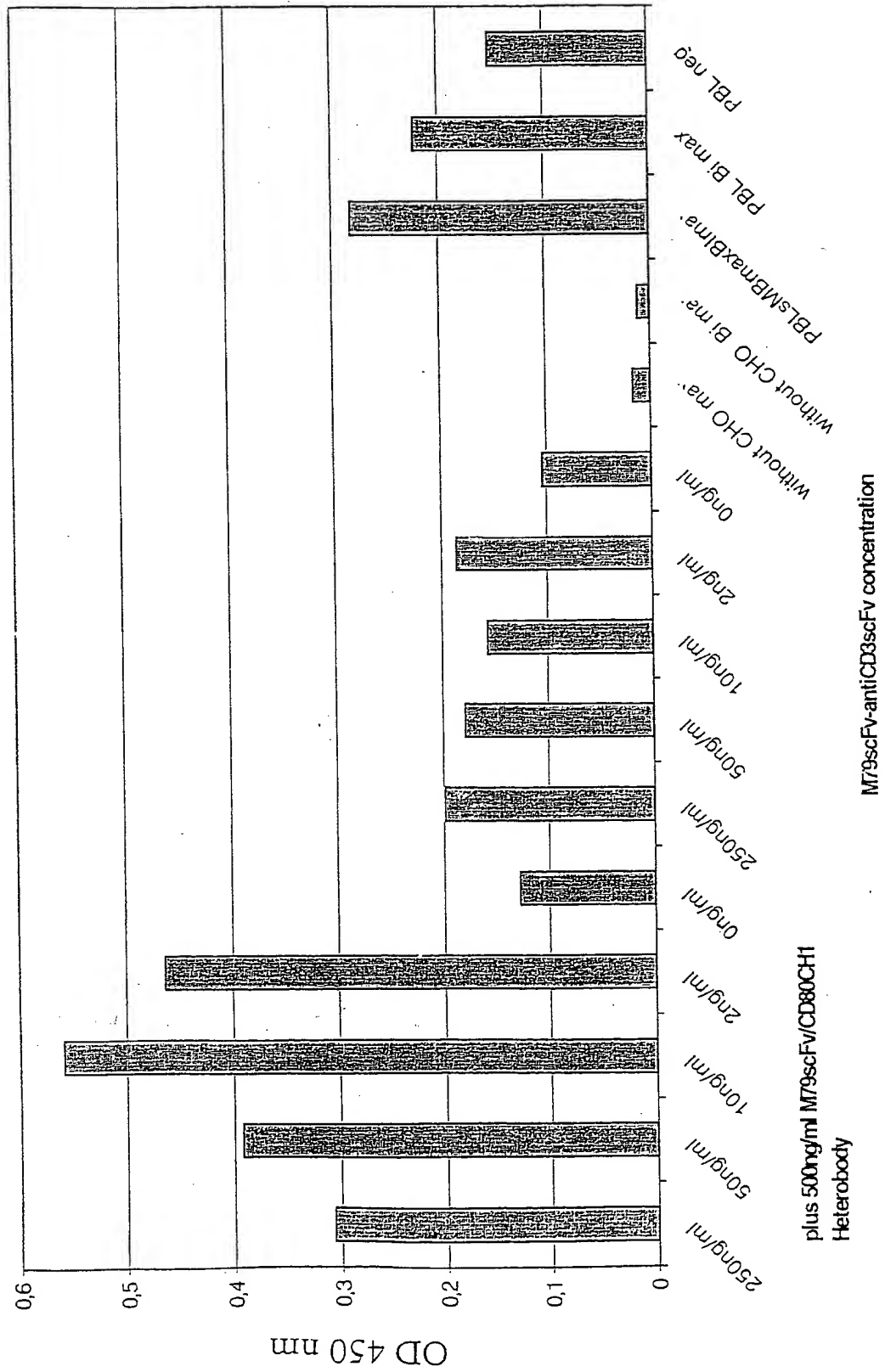
109720-5294460

OD405nm



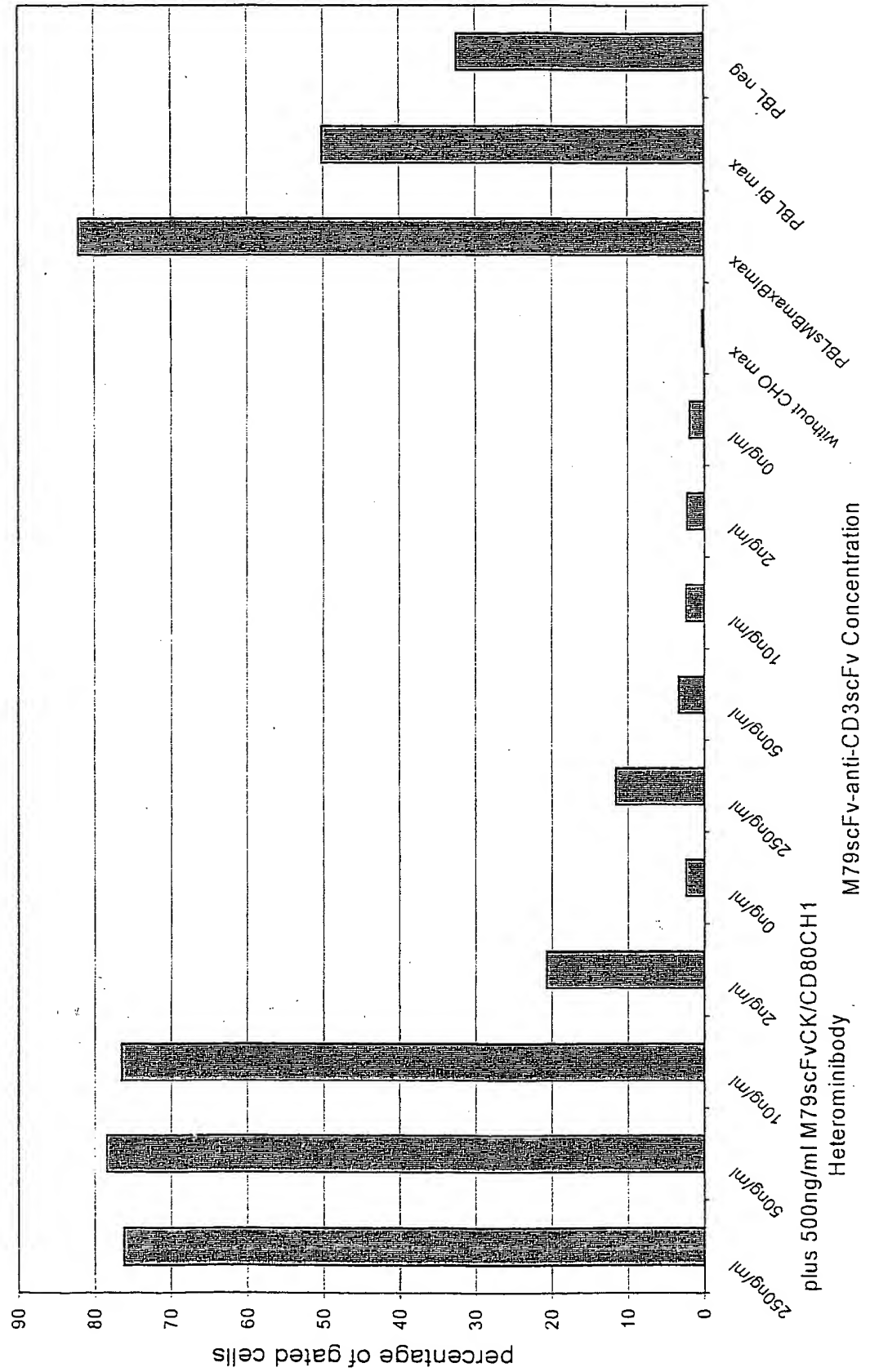
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Figure 19



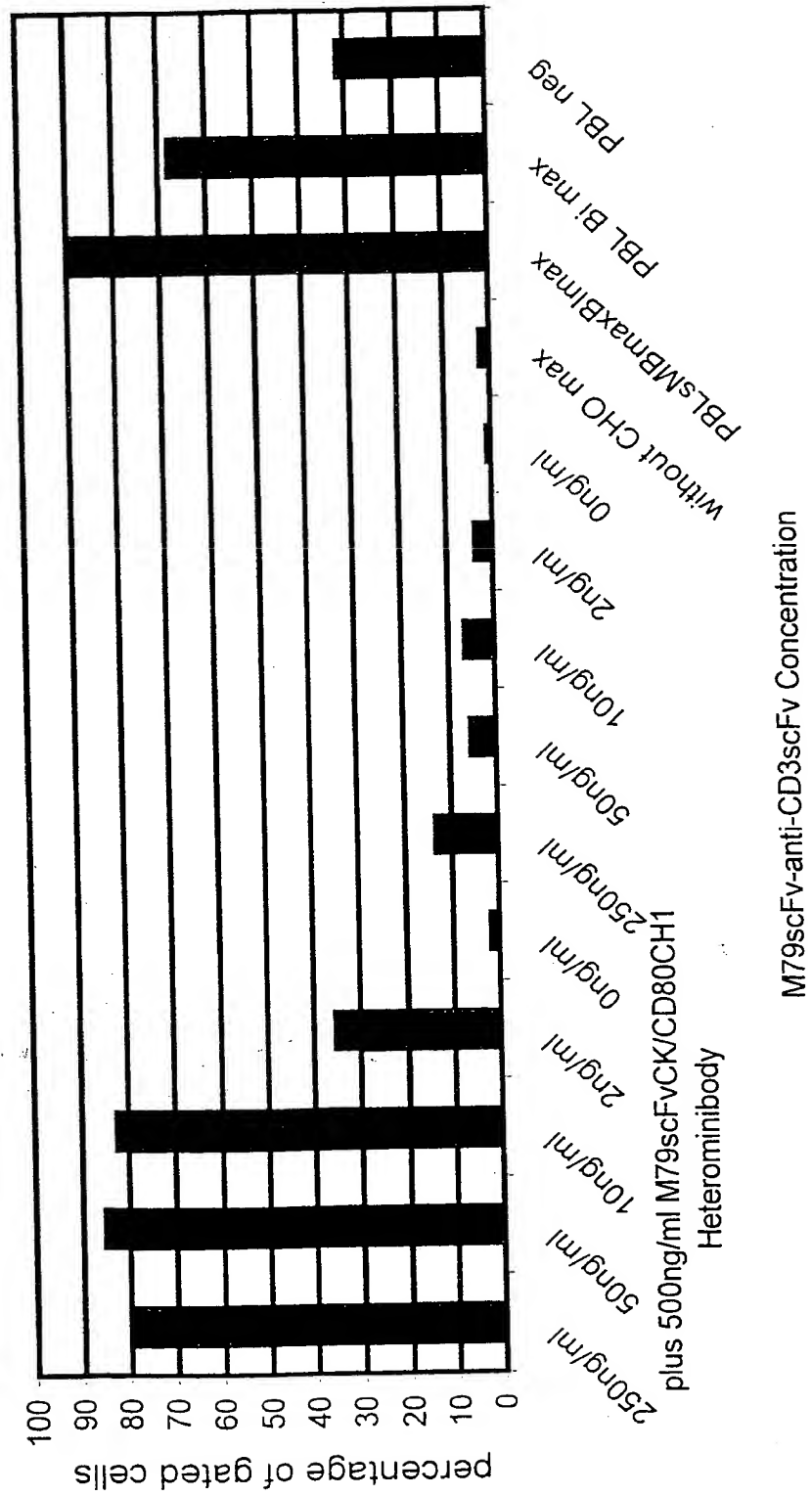
25/75

Figure 20

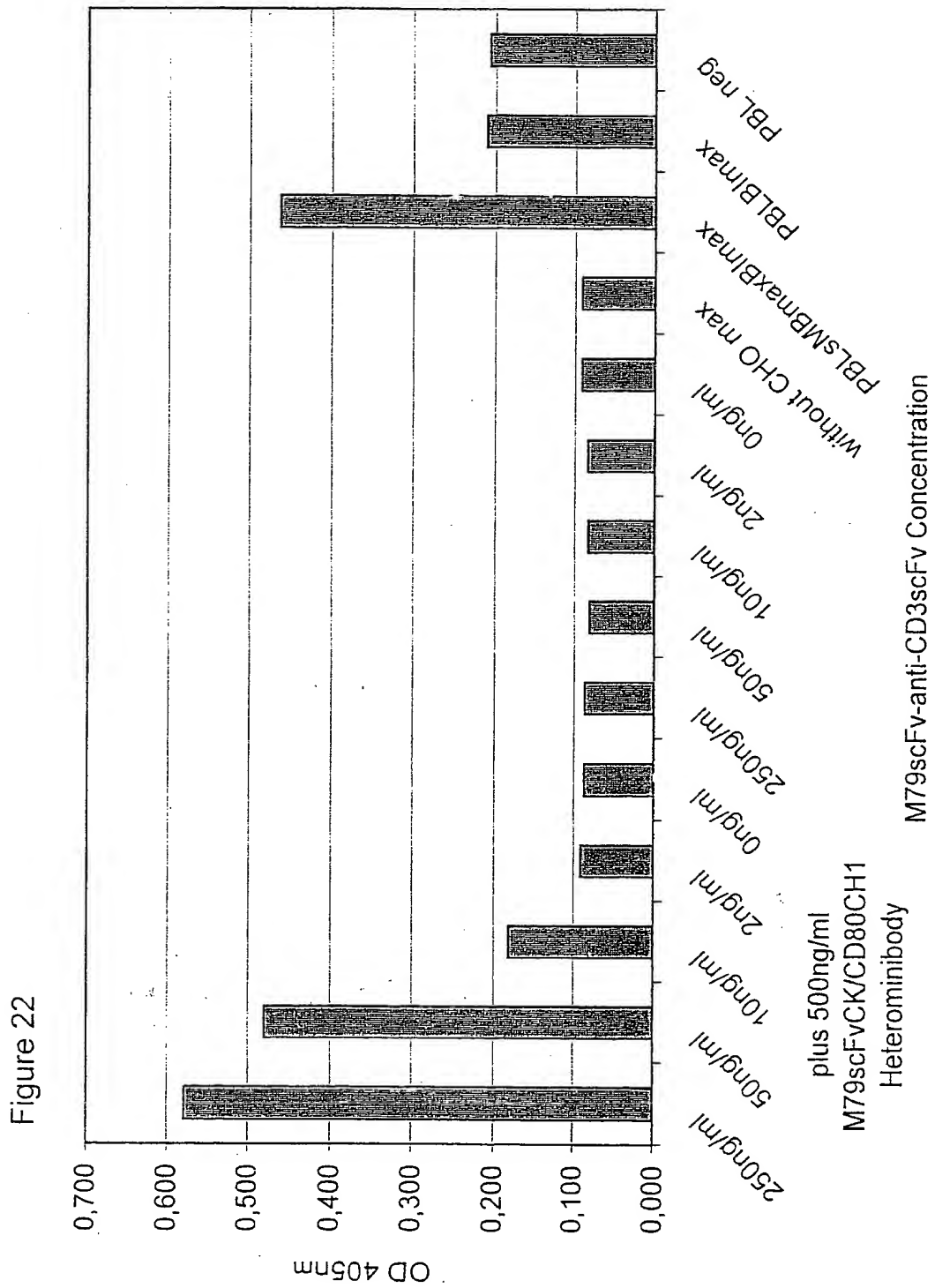


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Figure 21

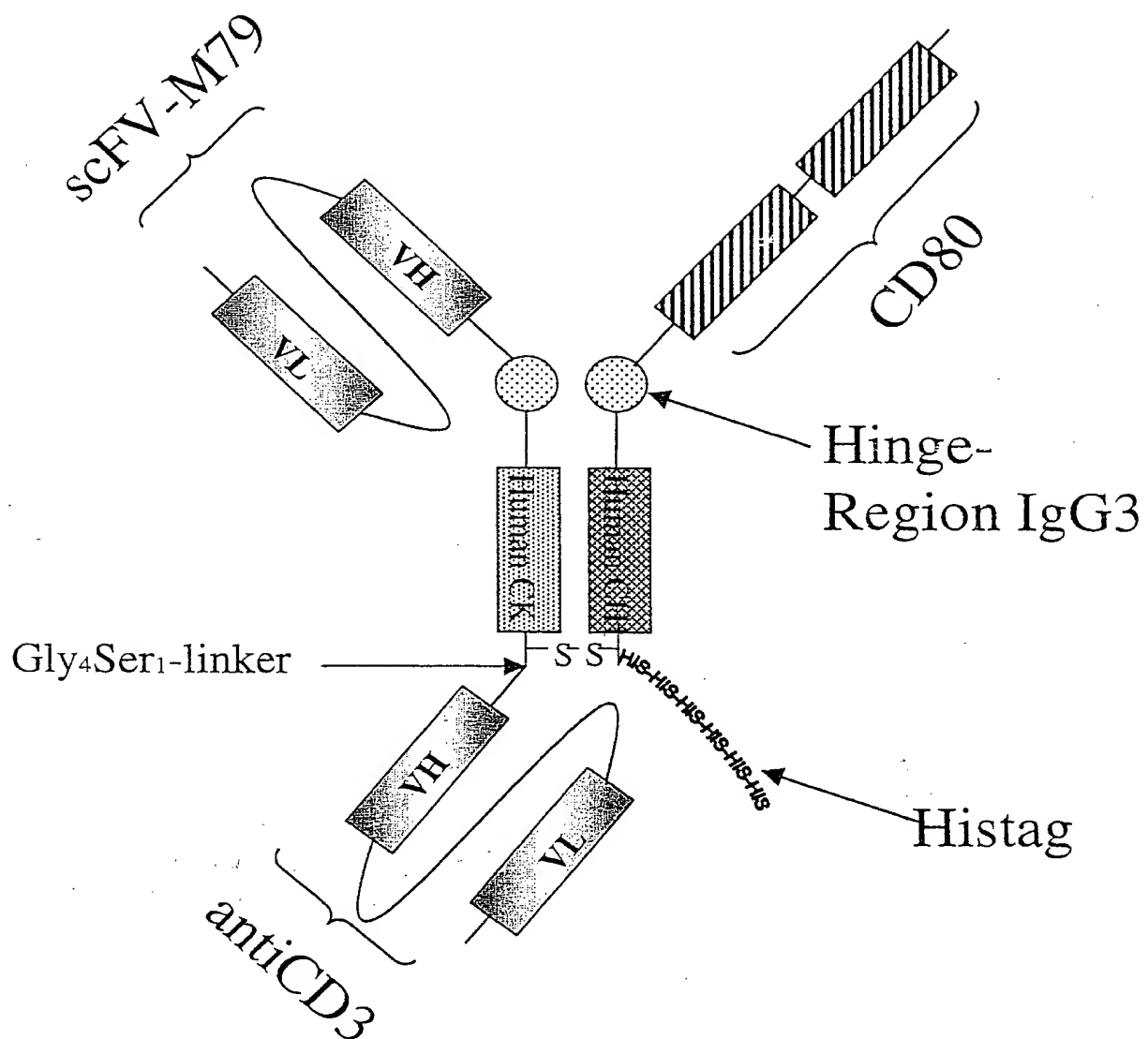


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Figure 23



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Figure 24

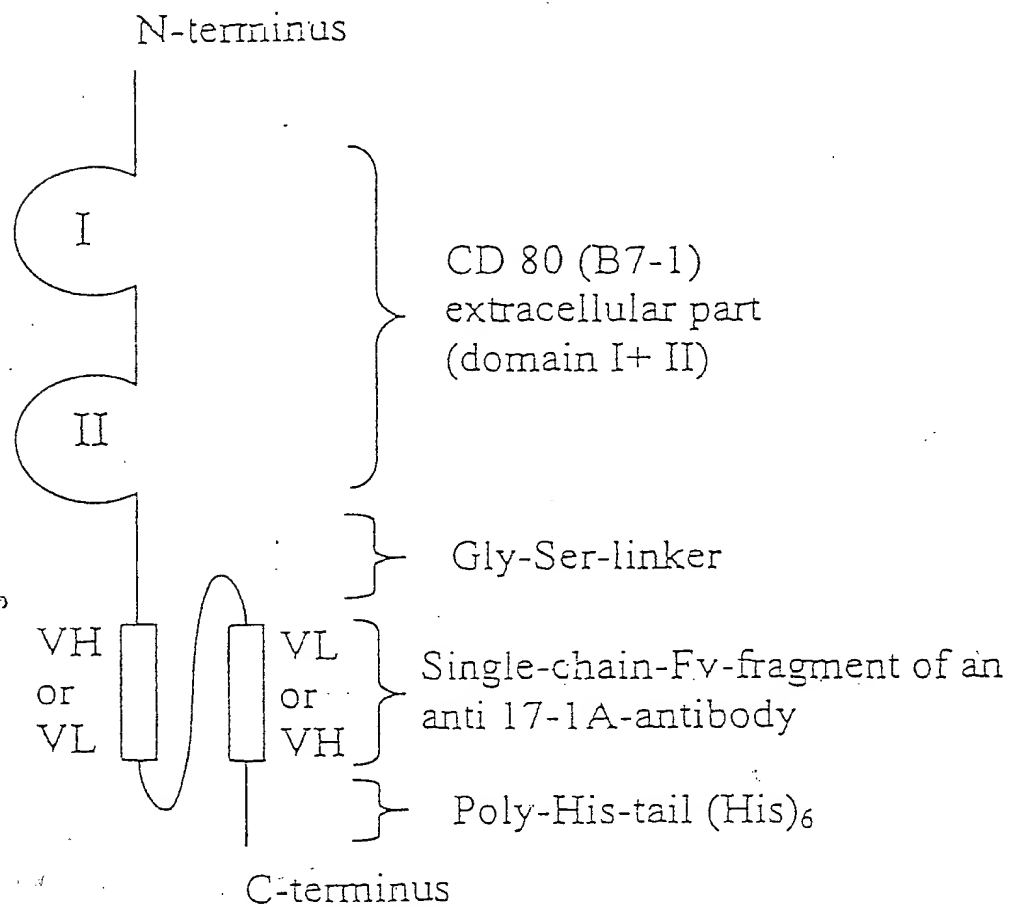
Recombinant bifunctional single-chain protein

Figure 25

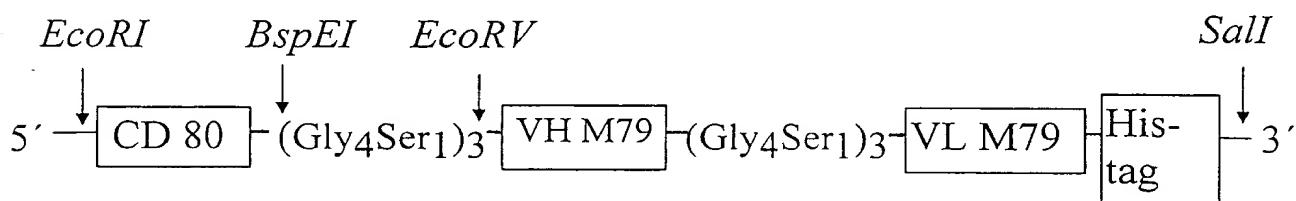
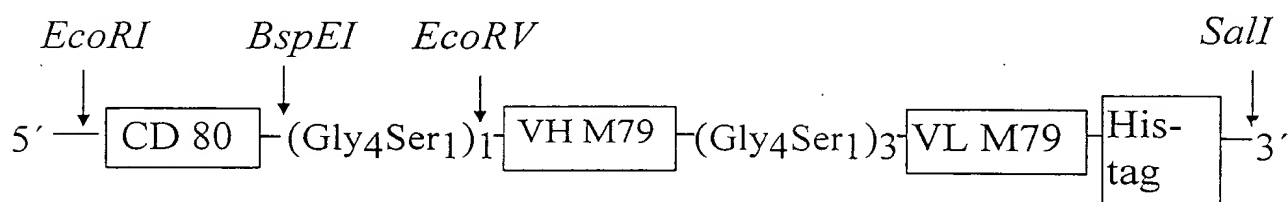
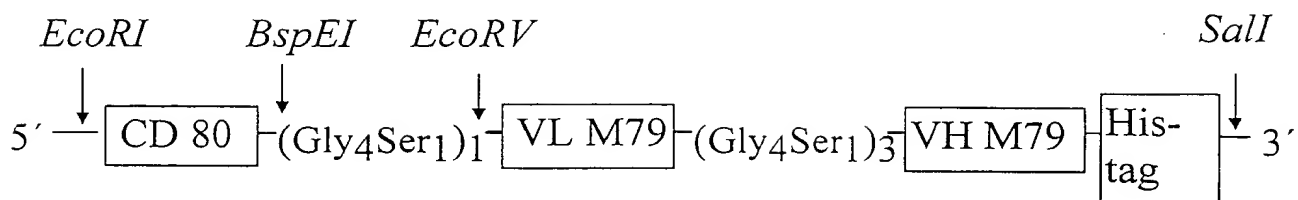


Figure 26

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ELISA-analysis
CD80-M79scFv (VL/VH) with short linker
Detection: anti-His-tag

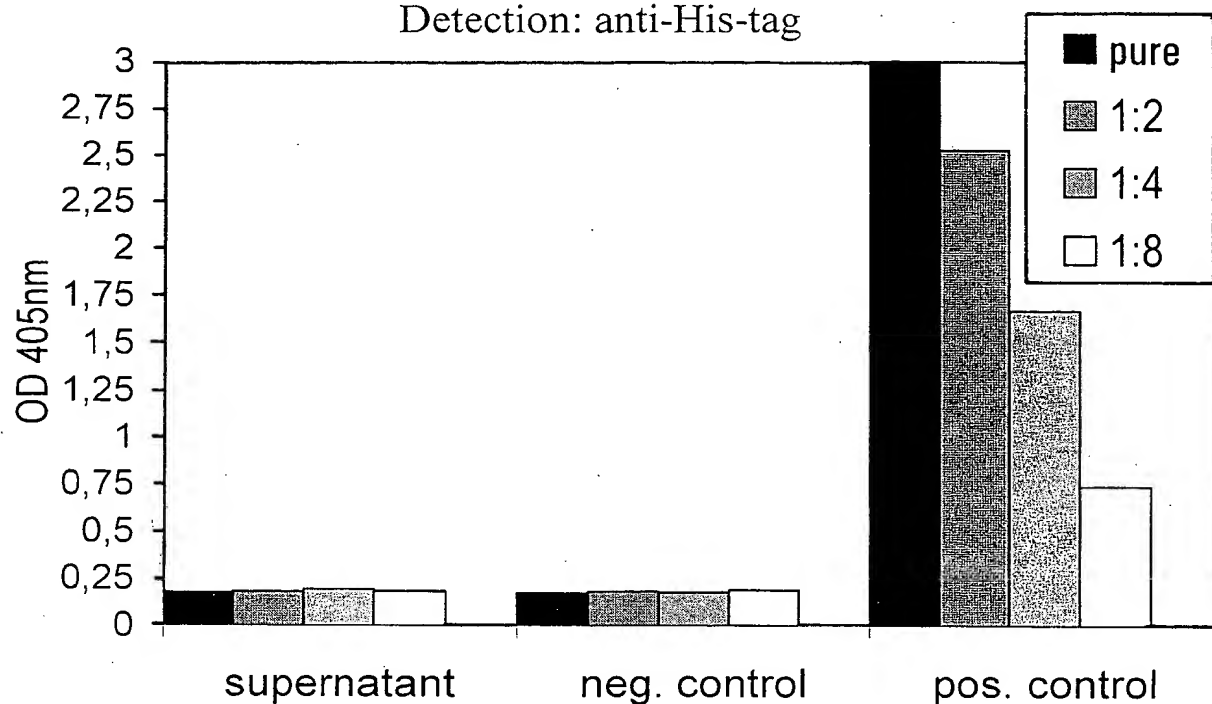
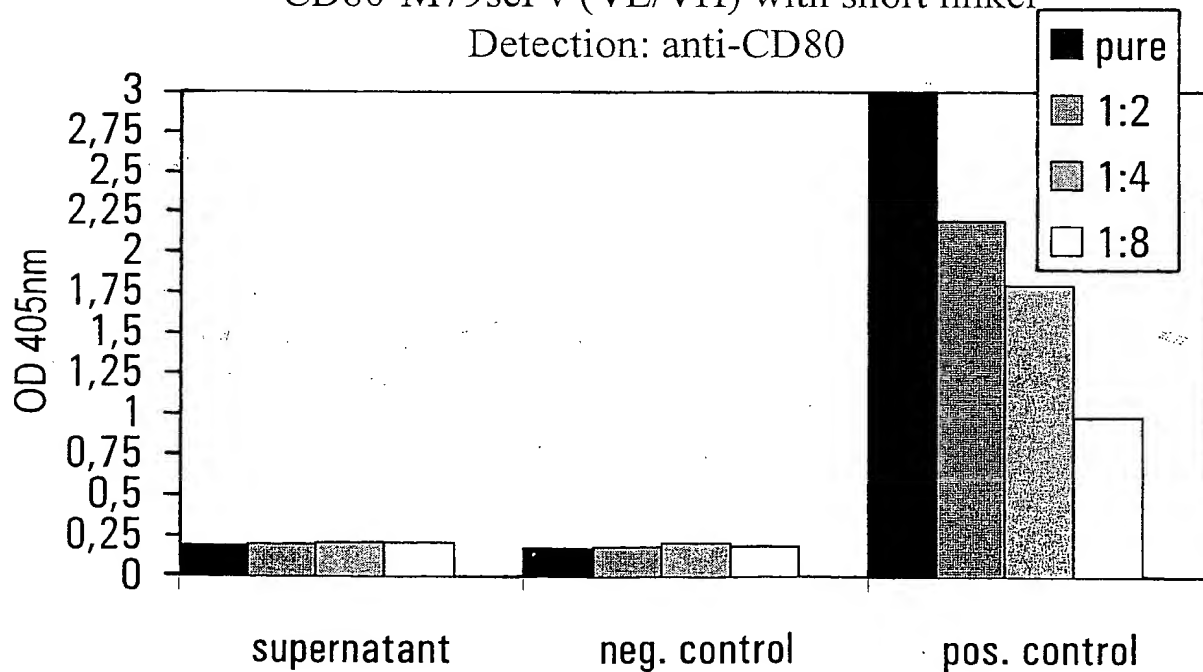


Figure 27

ELISA-analysis
CD80-M79scFv (VL/VH) with short linker
Detection: anti-CD80



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Figure 28

ELISA-analysis

CD80-M79scFv (VL/VH) with short linker

Detection: anti-His-tag or anti-CD80 (as indicated)

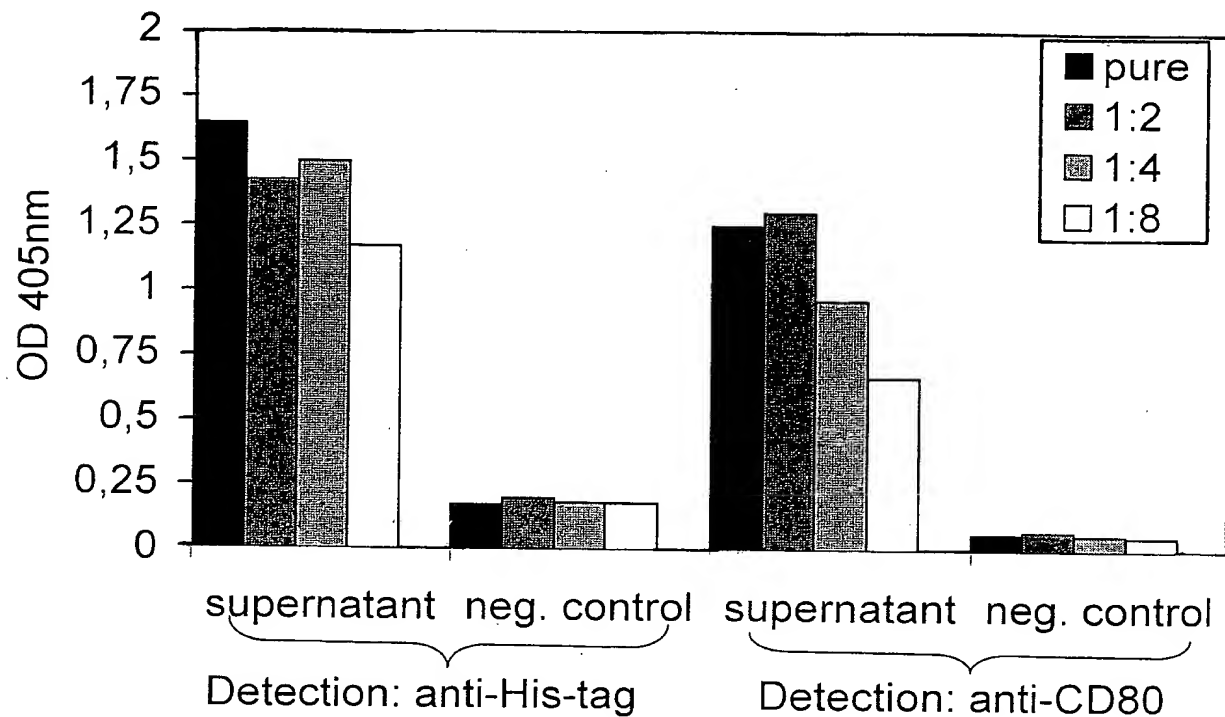


Figure 29

ELISA-analysis

CD80-M79 scFv (VH/VL) with short linker

Detection: anti-CD80

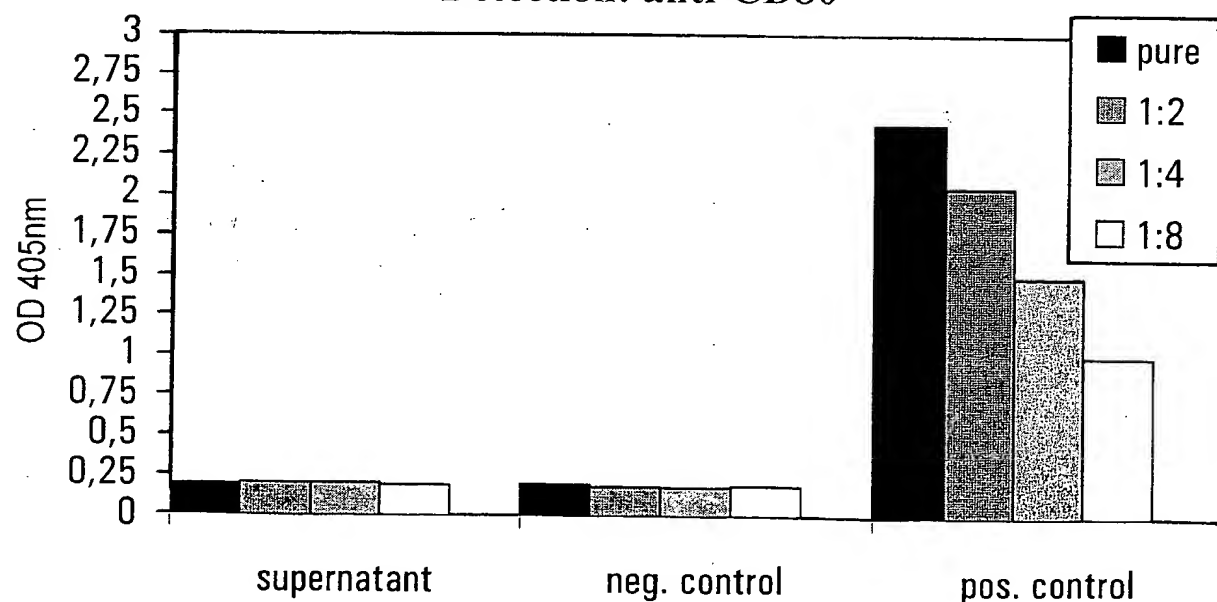
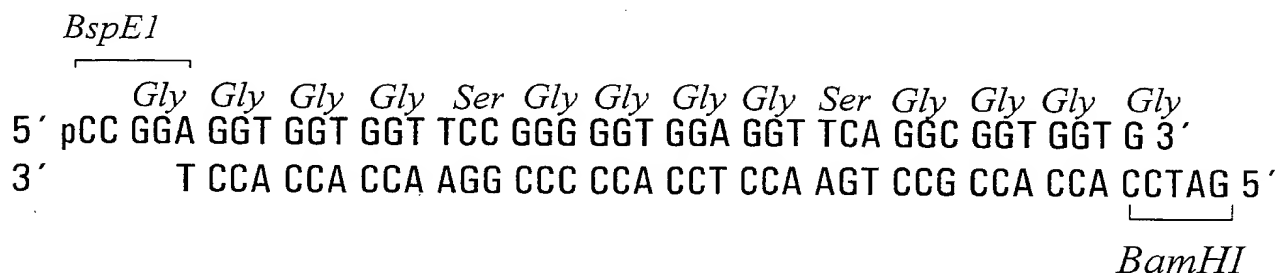


Figure 30

DNA-sequence of the double-stranded oligonucleotide designated ACCGS15 BAM

**Figure 31**

ELISA-analysis
CD80-M79scFv (VH/VL) with long linker
Detection: anti-His-tag

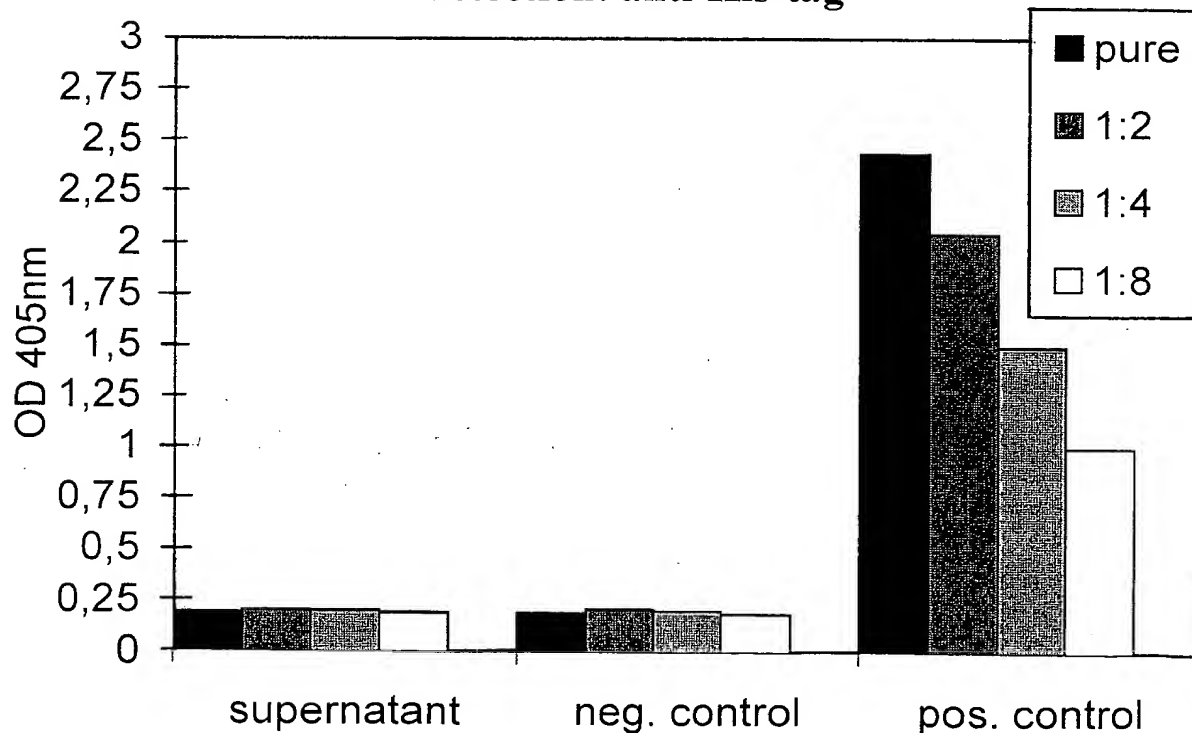


Figure 32

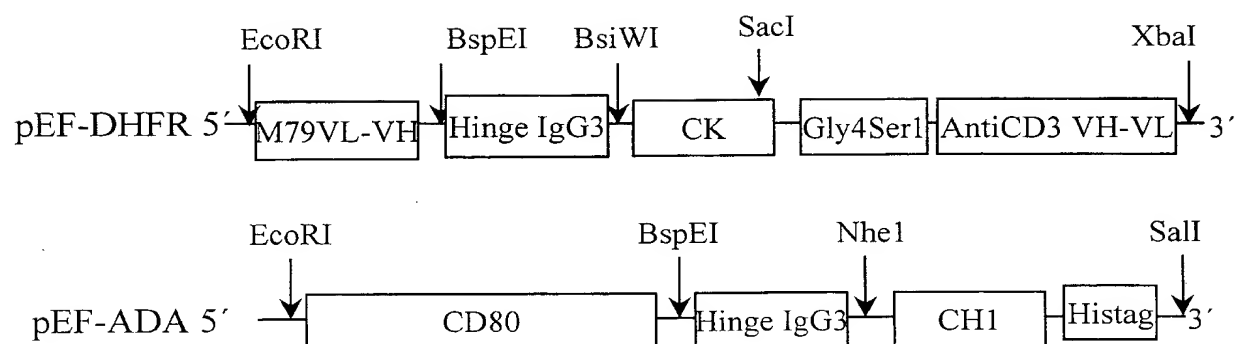
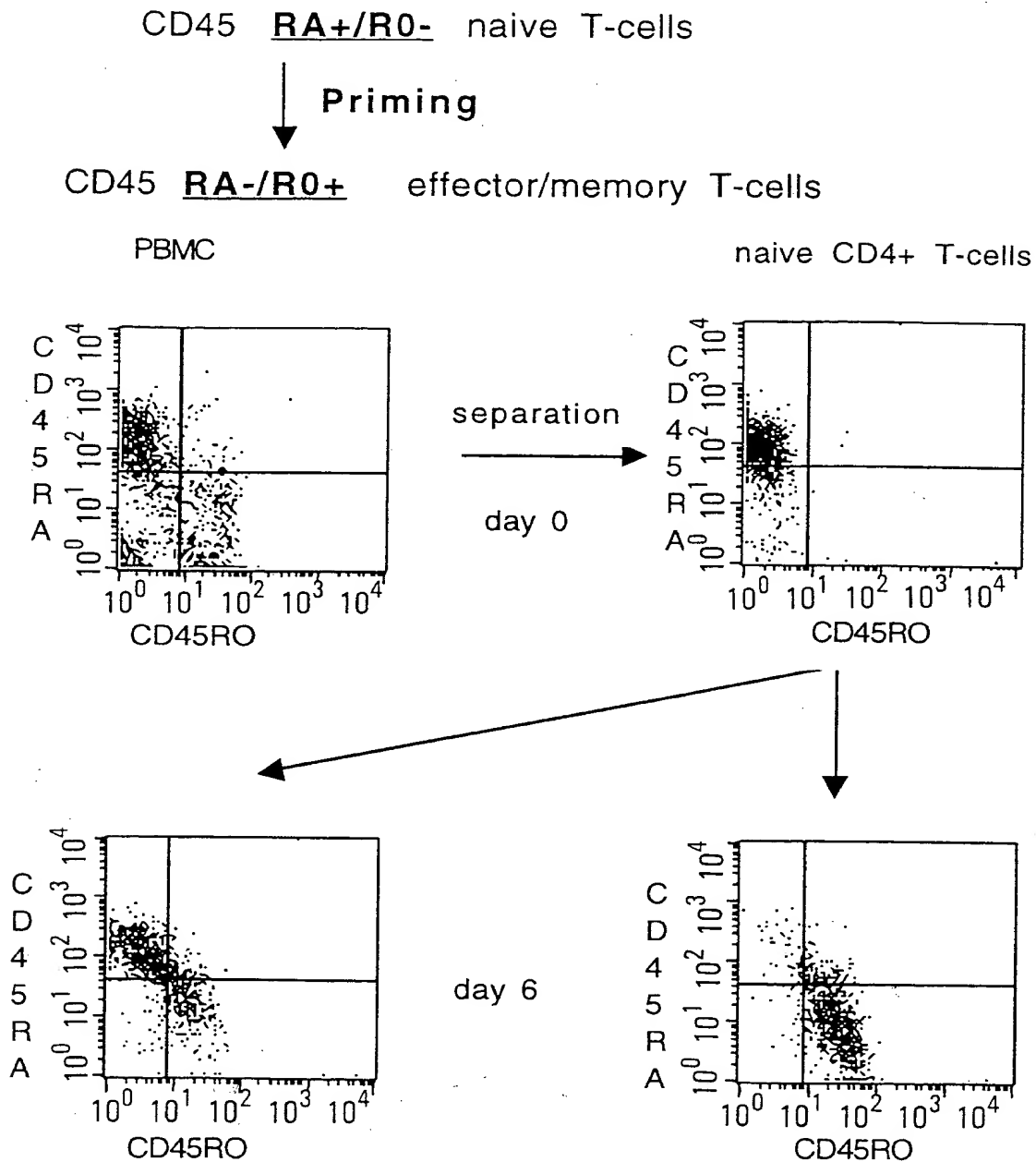


Figure 33 ^{35/75} Phenotyp-Switch

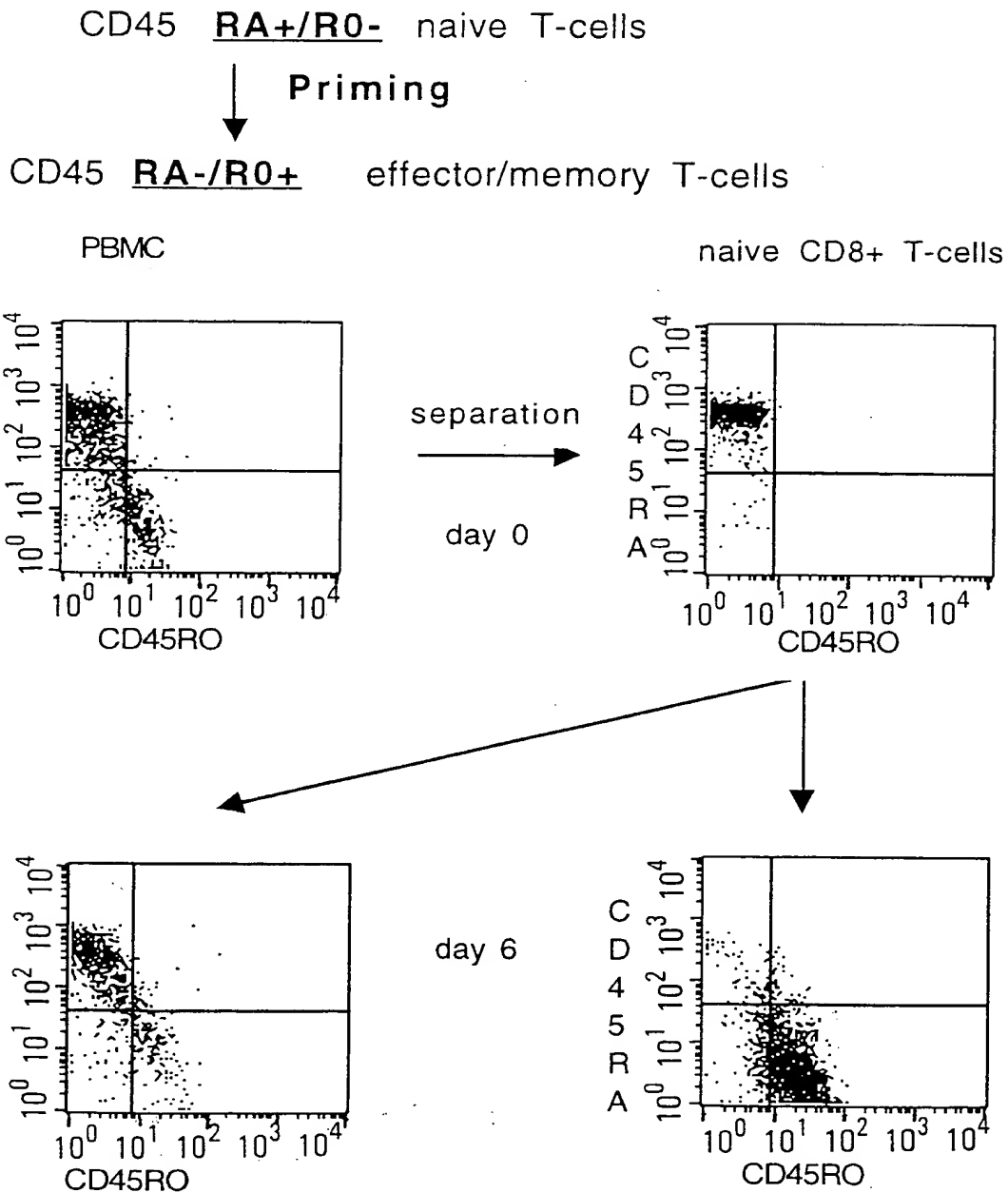


only primary signal:
M79scFv-antiCD3scFv

primary + costimulatory signal:
M79scFv-antiCD3scFv and
M79scFvCK/CD80CH1
Heterominibody

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Figure 34 Phenotyp-Switch

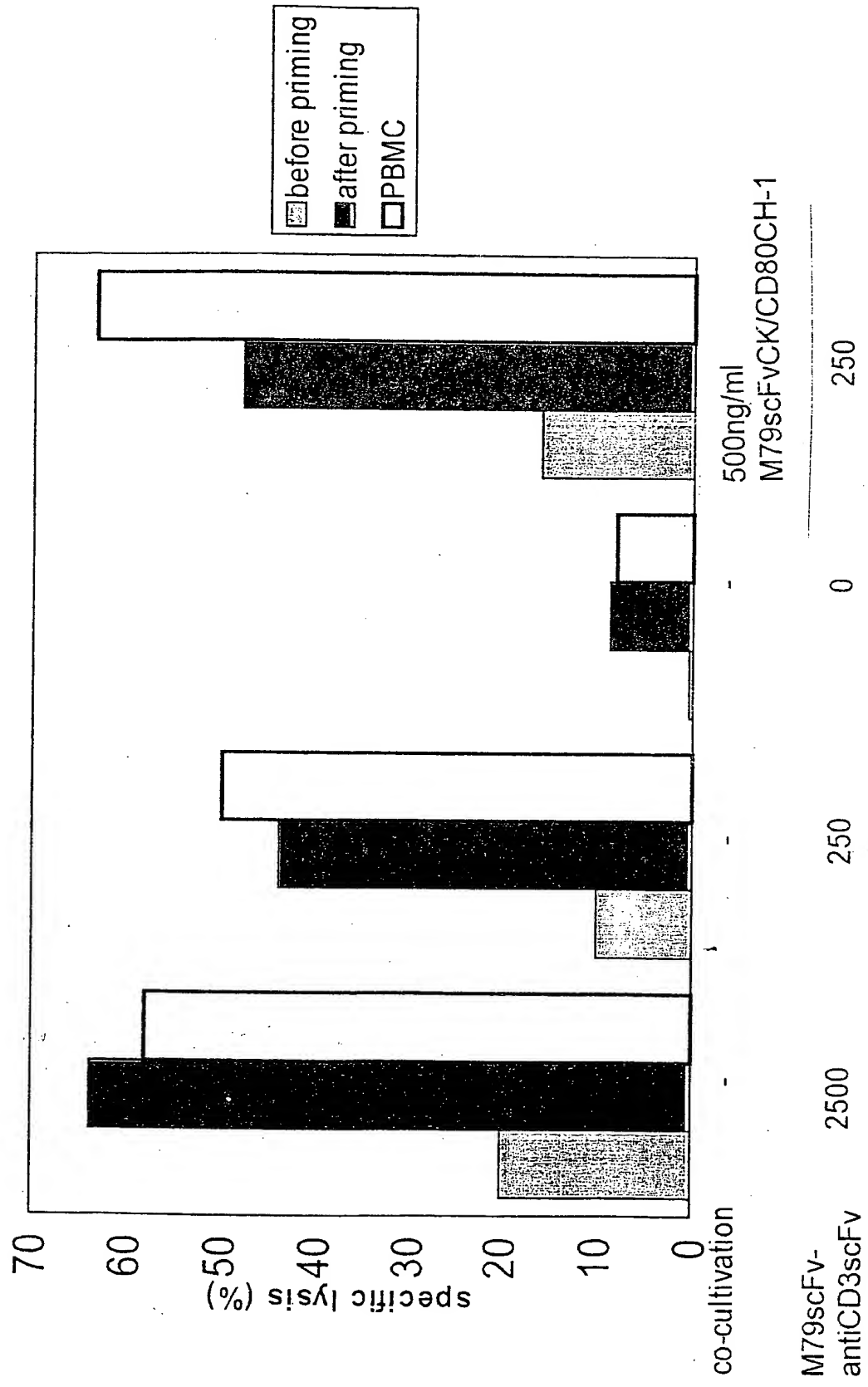


only primary signal:
M79scFv-antiCD3scFv

primary + costimulatory signal:
M79scFv-antiCD3scFv and
M79scFvCK/CD80CH1
Heterominibody

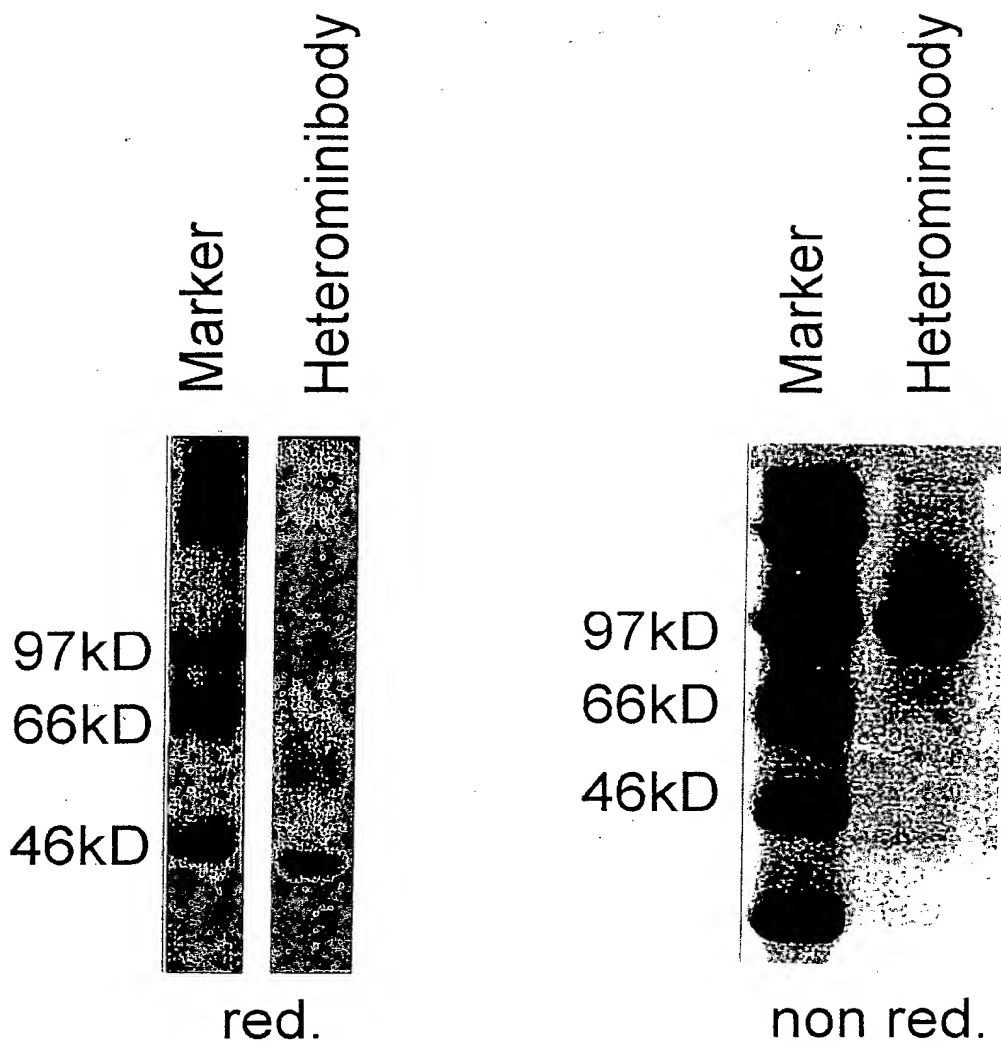
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Figure35



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Figure 36



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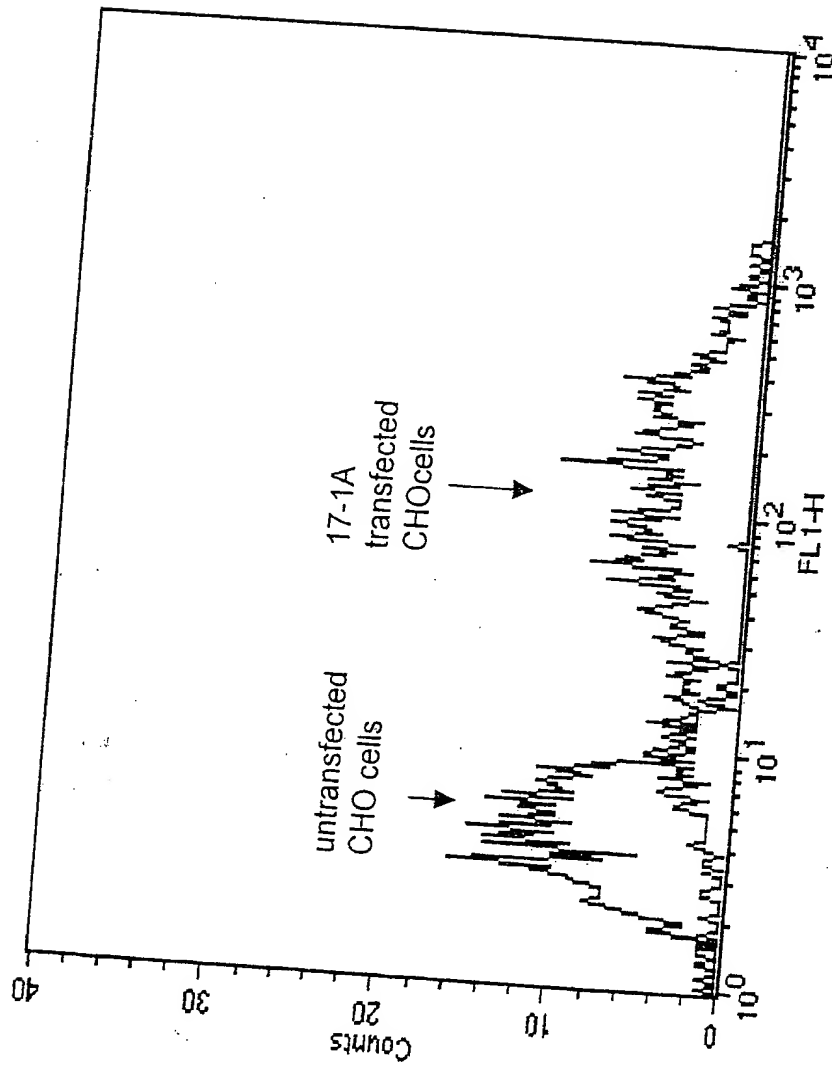


Figure 37

FO9F20 52944260

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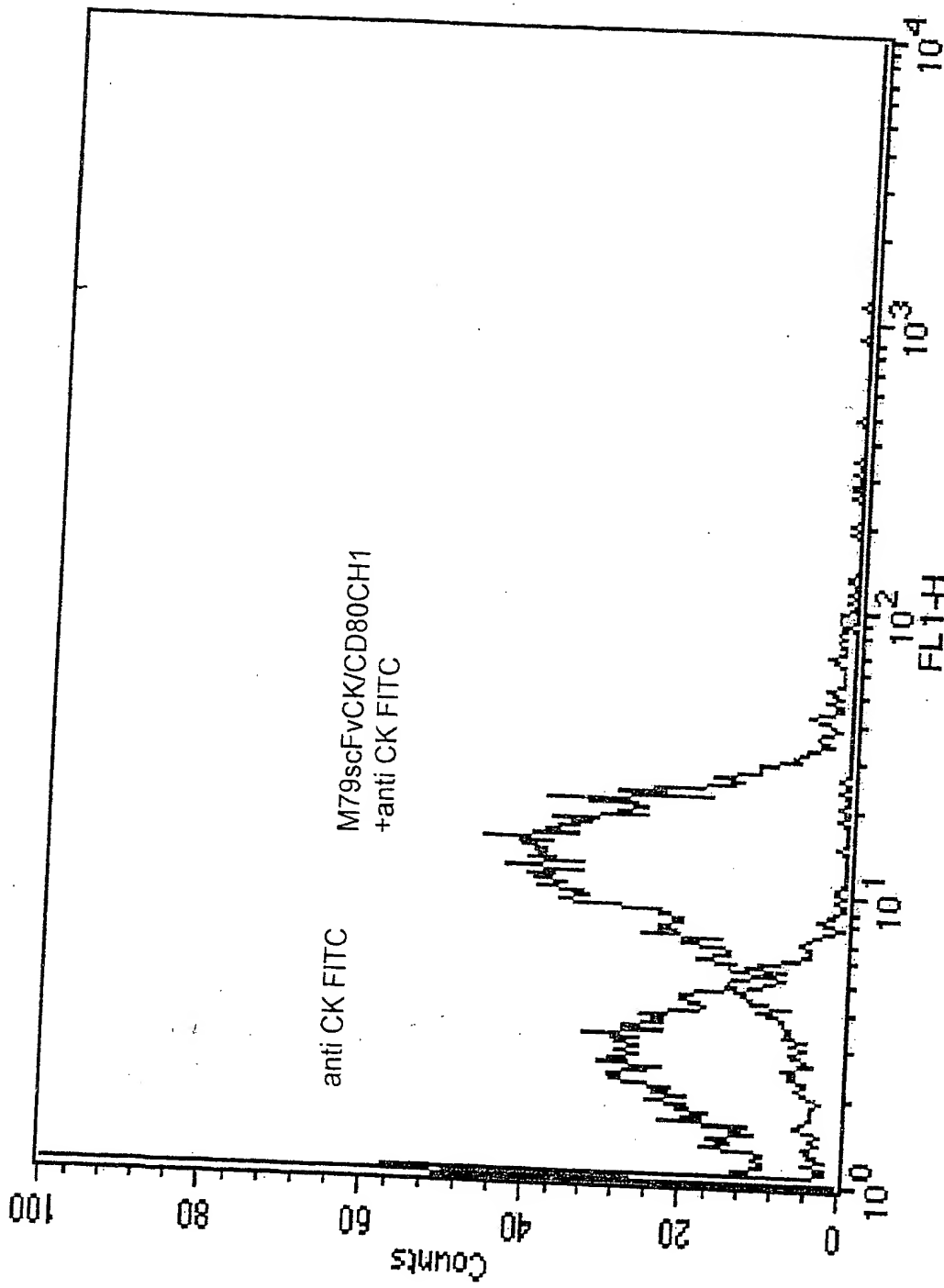


Figure 38

Figure 39

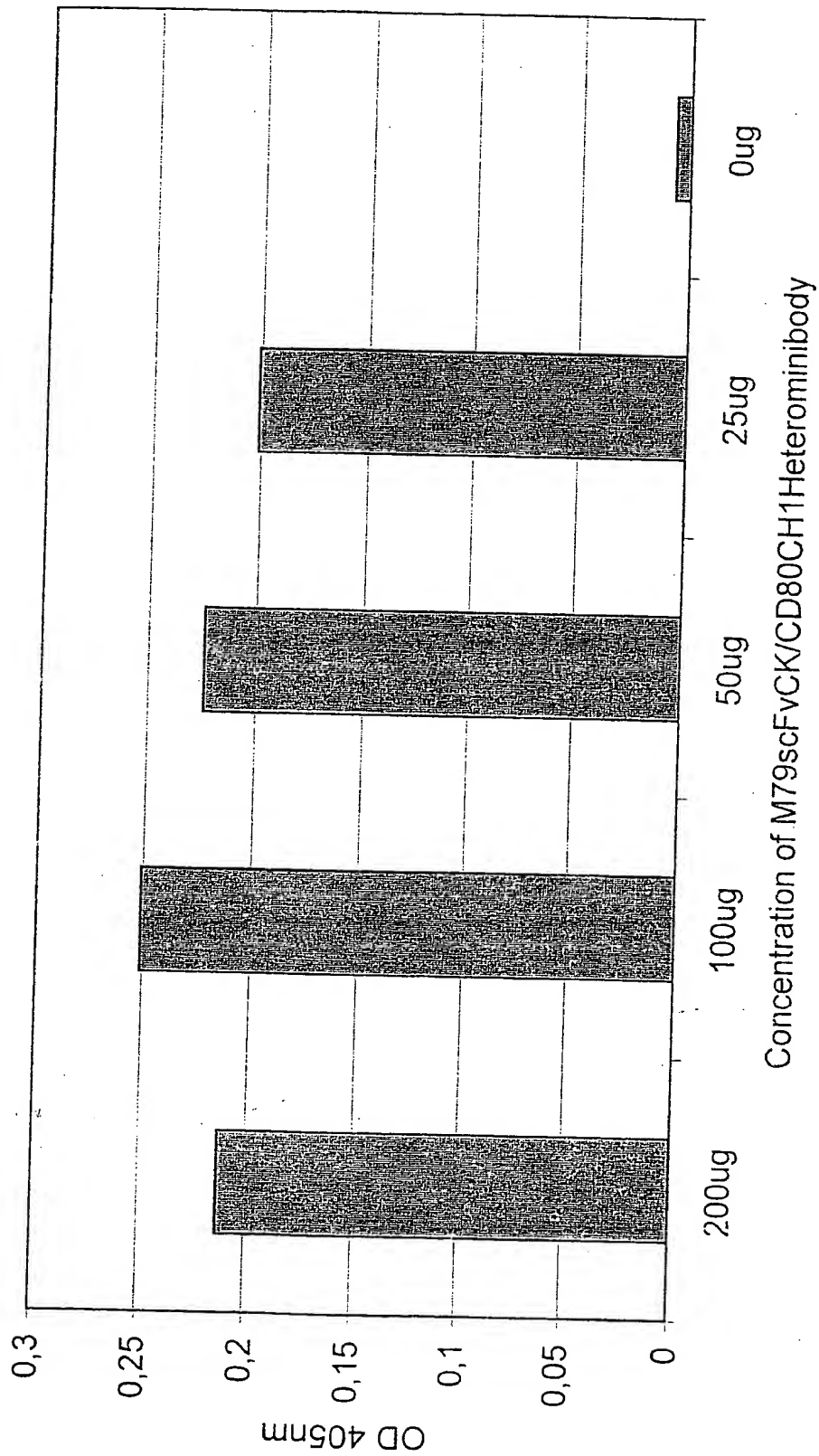


Figure 40

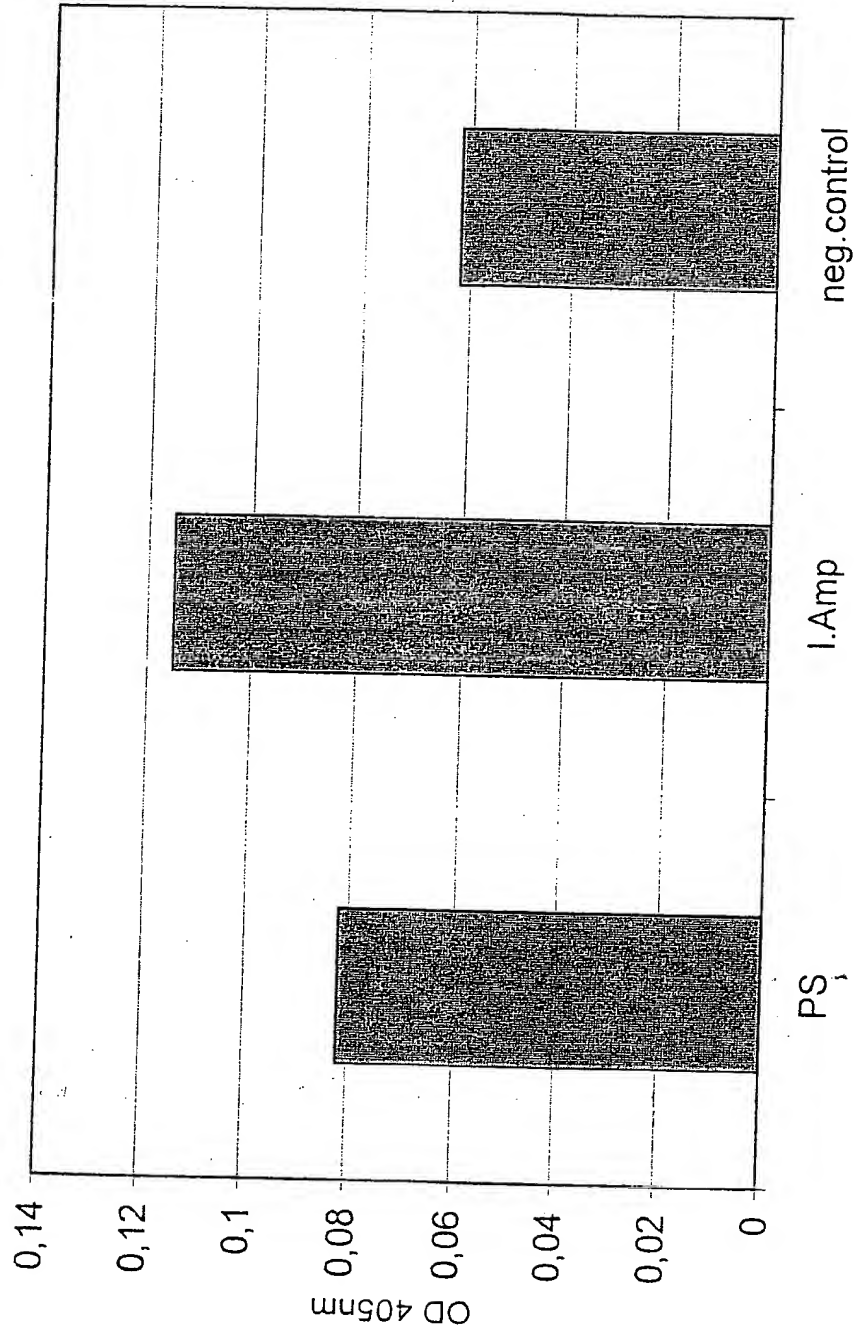


Figure 41

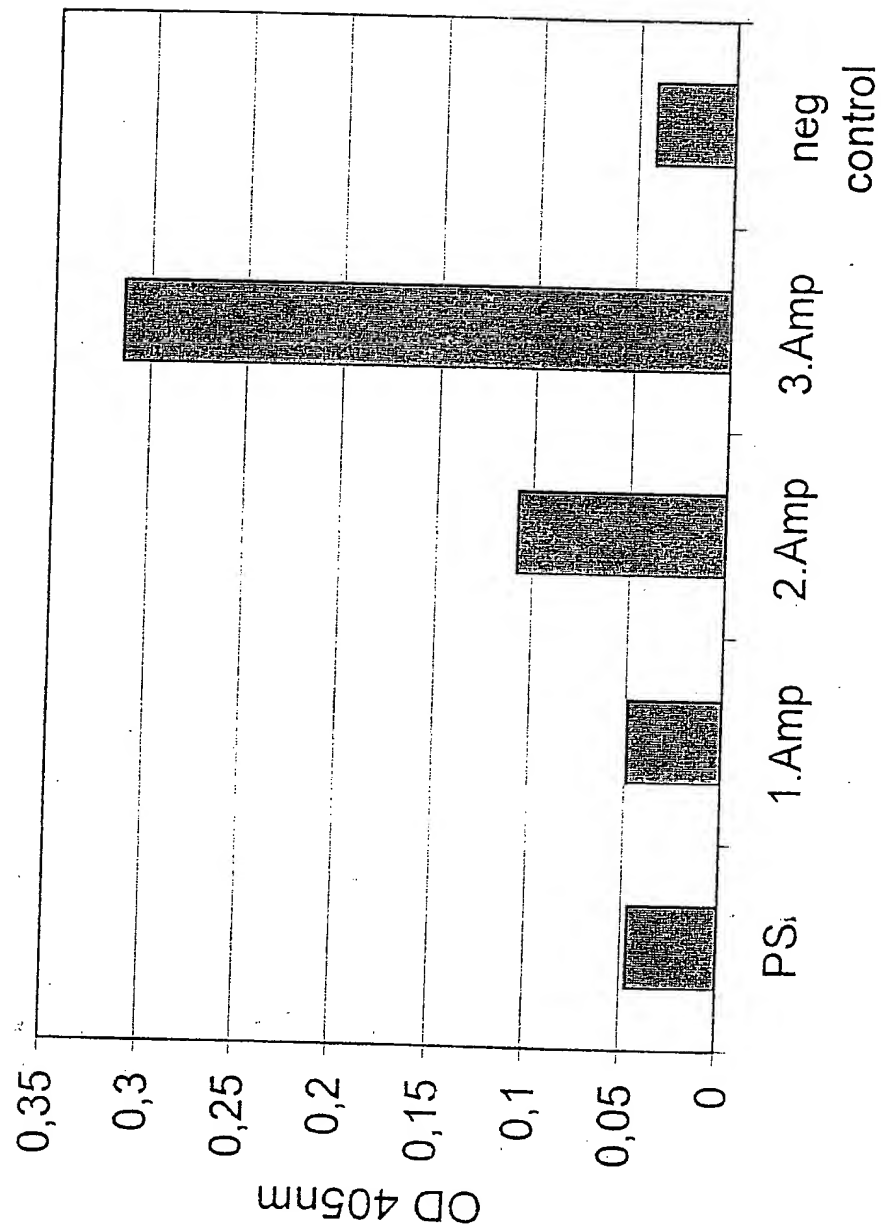
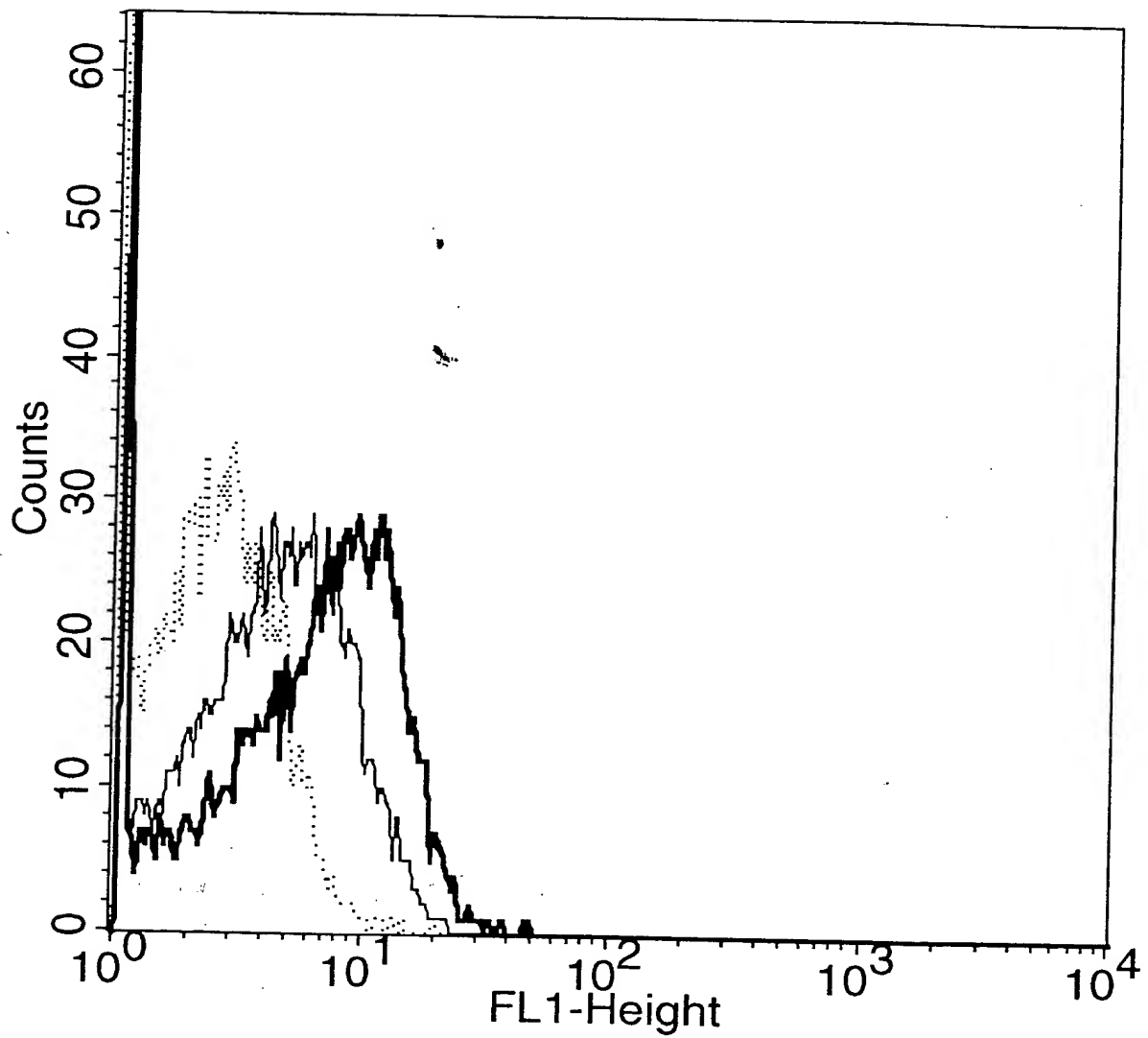


Figure 42



----- neg. control
—— 50µg/ml Heterominibody
—— 400µg/ml Heterominibody

Figure 43

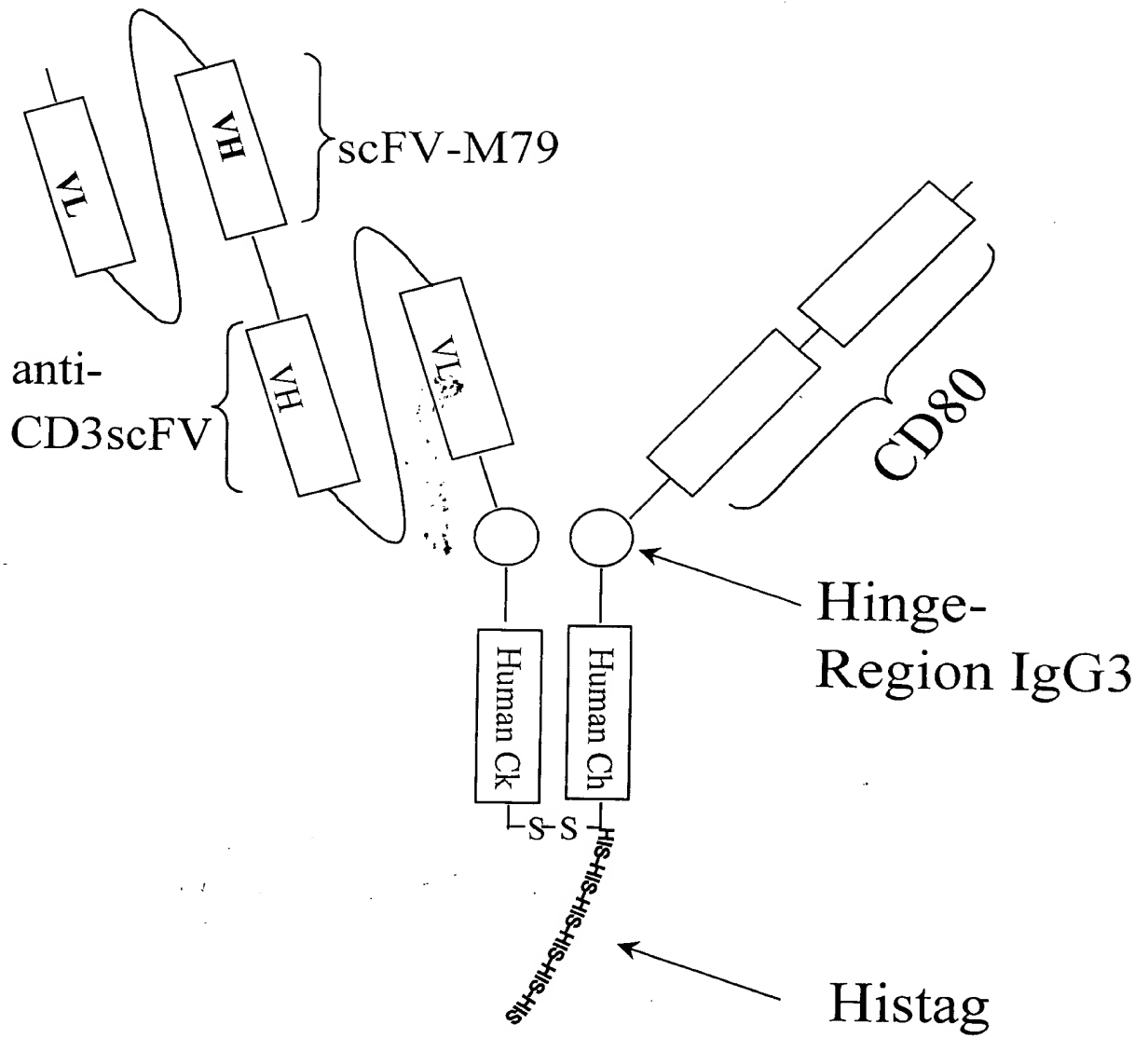
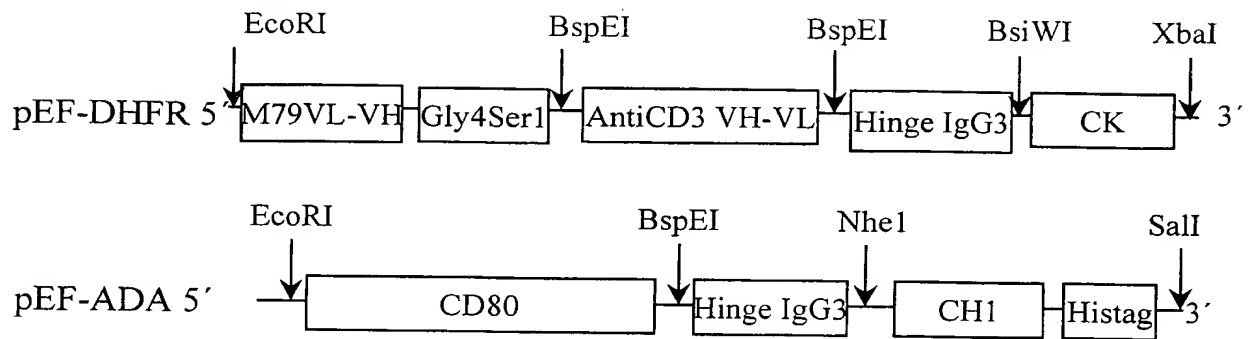


Fig 44



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Figure 45

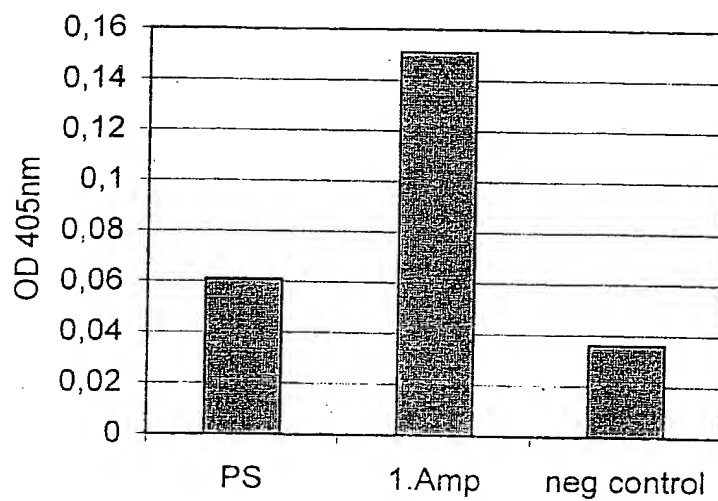
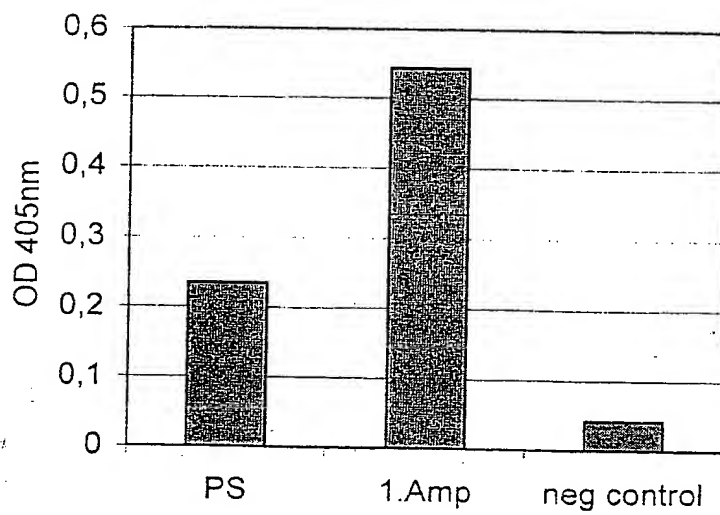


Figure 46



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Figure 47:

5'	EcoRI			9			18			27			36			45			54		
	GAA	TTC	ACC	ATG	GGA	TGG	AGC	TGT	ATC	ATC	CTC	TTC	TTG	GTA	GCA	ACA	GCT	ACA			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
				M	G	W	S	C	I	I	L	F	L	V	A	T	A	T			
	63			72			81			90			99			108					
	GGT	GTA	CAC	TCC	GAT	ATC	CAG	CTG	ACC	CAG	TCT	CAA	AAA	TTC	ATG	TCC	ACA	TCA			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	G	V	H	S	D	I	Q	L	T	Q	S	Q	K	F	M	S	T	S			
	117			126			135			144			153			162					
	GTA	GGA	GAC	AGG	GTC	AGC	GTC	ACC	TGC	AAG	GCC	AGT	CAG	AAT	GTG	GGT	ACT	AAT			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	V	G	D	R	V	S	V	T	C	K	A	S	Q	N	V	G	T	N			
	171			180			189			198			207			216					
	GTA	GCC	TGG	TAT	CAA	CAG	AAA	CCA	GCG	CAA	TCT	CCT	AAA	GCA	CTG	ATT	TAC	TCG			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	V	A	W	Y	Q	Q	K	P	G	Q	S	P	K	A	L	I	Y	S			
	225			234			243			252			261			270					
	GCA	TCC	TAC	CGG	TAC	AGT	GGA	GTC	CCT	GAT	CGC	TTC	ACA	GGC	AGT	GGA	TCT	GGG			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	A	S	Y	R	Y	S	G	V	P	D	R	F	T	G	S	G	S	G			
	279			288			297			306			315			324					
	ACA	GAT	TTC	ACT	CTC	ACC	ATC	AGC	AAT	GTG	CAG	TCT	GAA	GAC	TTG	GCA	CAG	TAT			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	T	D	F	T	L	T	I	S	N	V	Q	S	E	D	L	A	E	Y			
	333			342			351			360			369			378					
	TTC	TGT	CAG	CAA	TAT	AAC	AGC	TAT	CCG	CTC	ACG	TTC	GGT	GCT	GGG	ACC	AAG	CTC			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	F	C	Q	Q	Y	N	S	Y	P	L	T	F	G	A	G	T	K	L			
	387			396			405			414			423			432					
	GAG	ATC	AAA	GGT	GGT	GGT	GGT	TCT	GGC	GGC	GGC	GGC	TCC	GGT	GGT	GGT	GGT	TCT			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	E	I	K	G	G	G	G	S	G	G	G	G	S	G	G	G	G	S			
	441			450			459			468			477			486					
	CAG	GTG	AAA	CTG	CAG	GAG	TCA	GGA	CCT	GGC	CTA	GTG	CAG	CCC	TCA	CAG	AGC	CTG			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	Q	V	K	L	Q	E	S	G	P	G	L	V	Q	P	S	Q	S	L			
	495			504			513			522			531			540					
	TCC	ATC	ACC	TGC	ACA	GTC	TCT	GGT	TTC	TCA	TTA	ACT	AGC	TAT	GGT	GTA	CAC	TGG			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	S	I	T	C	T	V	S	G	F	S	L	T	S	Y	G	V	H	W			
	549			558			567			576			585			594					
	GTT	CGC	CAG	TCT	CCA	GGA	AAG	GGT	CTG	GAG	TGG	CTG	GGA	GTG	ATA	TGG	AGT	GGT			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	V	R	Q	S	P	G	K	G	L	E	W	L	G	V	I	W	S	G			
	603			612			621			630			639			648					
	GGA	AGC	ACA	GAC	TAT	AAT	GCA	GCT	TTC	ATA	TCC	AGA	CTG	AGC	ATC	AGC	AAG	GAC			
	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	G	S	T	D	Y	N	A	A	F	I	S	R	L	S	I	S	K	D			

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Figure 47 cont.

		657			666			675			684			693			702
AAT	TCC	AAG	AGC	CAA	GTT	TTC	TTT	AAA	ATG	AAC	AGT	CTG	CAA	GCT	AAT	GAC	ACA
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
N	S	K	S	Q	V	F	F	K	M	N	S	L	Q	A	N	D	T
		711			720			729			738			747			756
GCC	ATA	TAT	TAC	TGT	GCC	AGA	ATG	GAG	AAC	TGG	TCG	TTT	GCT	TAC	TGG	GGC	CAA
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
A	I	Y	Y	C	A	R	M	E	N	W	S	F	A	Y	W	G	Q
		765			774			783			792			801			810
GGG	ACC	ACG	GTC	ACC	GTC	TCC	GAA	TTC	CCC	AAA	CCT	AGC	ACC	CCC	CCT	GGC	AGC
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
G	T	T	V	T	V	S	E	F	P	K	P	S	T	P	P	G	S
		819			828			837			846			855			864
AGT	GGT	GAA	CTG	GAA	GAG	CTG	CTT	AAG	CAT	CTT	AAA	GAA	CTT	CTG	AAG	GGC	CCC
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
S	G	E	L	E	E	L	L	K	H	L	K	E	L	L	K	G	P
		873			882			891			900			909			918
CGC	AAA	GGC	GAA	CTC	GAG	GAA	CTG	CTG	AAA	CAT	CTG	AAG	GAG	CTG	CTT	AAA	GGT
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
R	K	G	E	L	E	E	L	L	K	H	L	K	E	L	L	K	G
		927			936			945			954			963			972
GGG	AGC	GGA	GGC	GCG	CCG	GCA	CCT	ACT	TCA	AGT	TCT	ACA	AAG	AAA	ACA	CAG	CTA
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
G	S	G	G	A	P	A	P	T	S	S	S	T	K	K	T	Q	L
		981			990			999			1008			1017			1026
CAA	CTG	GAG	CAT	TTA	CTG	CTG	GAT	TTA	CAG	ATG	ATT	TTG	AAT	GGA	ATT	AAT	AAT
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Q	L	E	H	L	L	L	D	L	Q	M	I	L	N	G	I	N	N
		1035			1044			1053			1062			1071			1080
TAC	AAG	AAT	CCC	AAA	CTC	ACC	AGG	ATG	CTC	ACA	TTT	AAG	TTT	TAC	ATG	CCC	AAG
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Y	K	N	P	K	L	T	R	M	L	T	F	K	F	Y	M	P	K
		1089			1098			1107			1116			1125			1134
AAG	GCC	ACA	GAA	CTG	AAA	CAT	CTT	CAG	TGT	CTA	GAA	GAA	GAA	CTC	AAA	CCT	CTG
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
K	A	T	E	L	K	H	L	Q	C	L	E	E	E	L	K	P	L
		1143			1152			1161			1170			1179			1188
GAG	GAA	GTG	CTA	AAT	TTA	GCT	CAA	AGC	AAA	AAC	TTT	CAC	TTA	AGA	CCC	AGG	GAC
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
E	E	V	L	N	L	A	Q	S	K	N	F	H	L	R	P	R	D
		1197			1206			1215			1224			1233			1242
TTA	ATC	AGC	AAT	ATC	AAC	GTA	ATA	GTT	CTG	GAA	CTA	AAG	GGA	TCT	GAA	ACA	ACA
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
L	I	S	N	I	N	V	I	V	L	E	L	K	G	S	E	T	T
		1251			1260			1269			1278			1287			1296
TTC	ATG	TGT	GAA	TAT	GCT	GAT	GAG	ACA	GCA	ACC	ATT	GTA	GAA	TTT	CTG	AAC	AGA
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
F	M	C	E	Y	A	D	E	T	A	T	I	V	E	F	L	N	R

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Figure 47 cont.

1305			1314				1323		1332			1341		1350			
TGG	ATT	ACC	TTT	TGT	CAA	AGC	ATC	ATC	TCA	ACA	CTG	ACT	GAC	GTC	CAT	CAC	CAT
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
W	I	T	F	C	Q	S	I	I	S	T	L	T	D	V	H	H	H
				SalI													
1359																	
CAC	CAT	CAC	TGA	TAA	GTC	GAC											
---	---	---	---	---	---	---											
H	H	H	*	*													

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EcoRI																			
5'	GAA	TTC	ACC	ATG	GGA	TGG	AGC	TGT	ATC	ATC	CTC	TTC	TTG	GTA	GCA	ACA	GCT	ACA	
				M	G	W	S	C	I	I	L	F	L	V	A	T	A	T	
	GGT	GTA	CAC	TCC	GAT	ATC	CAG	CTG	ACC	CAG	TCT	CAA	AAA	TTC	ATG	TCC	ACA	TCA	
	G	V	H	S	D	I	Q	L	T	Q	S	Q	K	F	M	S	T	S	
	GTA	GGA	GAC	AGG	GTC	AGC	GTC	ACC	TGC	AAG	GCC	AGT	CAG	AAT	GTG	GGT	ACT	AAT	
	V	G	D	R	V	S	V	T	C	K	A	S	Q	N	V	G	T	N	
	GTA	GCC	TGG	TAT	CAA	CAG	AAA	CCA	GGG	CAA	TCT	CCT	AAA	GCA	CTG	ATT	TAC	TCG	
	V	A	W	Y	Q	Q	K	P	G	Q	S	P	K	A	L	I	Y	S	
	GCA	TCC	TAC	CGG	TAC	AGT	GGA	GTC	CCT	GAT	CGC	TTC	ACA	GGC	AGT	GGA	TCT	GGG	
	A	S	Y	R	Y	S	G	V	P	D	R	F	T	G	S	G	S	G	
	ACA	GAT	TTC	ACT	CTC	ACC	ATC	AGC	AAT	GTG	CAG	TCT	GAA	GAC	TTG	GCA	GAG	TAT	
	T	D	F	T	L	T	I	S	N	V	Q	S	E	D	L	A	E	Y	
	TTC	TGT	CAG	CAA	TAT	AAC	AGC	TAT	CCG	CTC	ACG	TTC	GGT	GCT	GGG	ACC	AAG	CTC	
	F	C	Q	Q	Y	N	S	Y	P	L	T	F	G	A	G	T	K	L	
	GAG	ATC	AAA	GGT	GGT	GGT	GGT	TCT	GGC	GGC	GGC	GGC	TCC	GGT	GGT	GGT	GGT	TCT	
	E	I	K	G	G	G	G	S	G	G	G	G	S	G	G	G	G	S	
	CAG	GTG	AAA	CTG	CAG	GAG	TCA	GGA	CCT	GGC	CTA	GTG	CAG	CCC	TCA	CAG	AGC	CTG	
	Q	V	K	L	Q	E	S	G	P	G	L	V	Q	P	S	Q	S	L	
	TCC	ATC	ACC	TGC	ACA	GTC	TCT	GGT	TTC	TCA	TTA	ACT	AGC	TAT	GGT	GTA	CAC	TGG	
	S	I	T	C	T	V	S	G	F	S	L	T	S	Y	G	V	H	W	
	GTT	CGC	CAG	TCT	CCA	GGA	AAG	GGT	CTG	GAG	TGG	CTG	GGA	GTG	ATA	TGG	AGT	GGT	
	V	R	Q	S	P	G	K	G	L	E	W	L	G	V	I	W	S	G	
	GGA	AGC	ACA	GAC	TAT	AAT	GCA	GCT	TTC	ATA	TCC	AGA	CTG	AGC	ATC	AGC	AAG	GAC	
	G	S	T	D	Y	N	A	A	F	I	S	R	L	S	I	S	K	D	

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Figure 48 cont.

AAT	TCC	657	AAG	AGC	CAA	666	GTT	TTC	TTT	675	AAA	ATG	AAC	684	AGT	CTG	CAA	693	GCT	AAT	GAC	702	ACA
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
N	S	K	S	Q	V	F	F	K	M	N	S	L	Q	A	N	D	T						
		711				720				729				738				747					756
GCC	ATA	TAT	TAC	TGT	GCC	AGA	ATG	GAG	AAC	TGG	TCG	TTT	GCT	TAC	TGG	GGC	CAA						
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
A	I	Y	Y	C	A	R	M	E	N	W	S	F	A	Y	W	G	Q						
		765				774				783				792				801					810
GGG	ACC	ACG	GTC	ACC	GTC	TCC	GAA	TTC	ACC	CCG	CTG	GGT	GAC	ACC	ACC	CAC	ACC						
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
G	T	T	V	T	V	S	E	F	T	P	L	G	D	T	T	H	T						
		819				828				837				846				855					864
TCC	GGA	AAA	CCA	CTG	GAT	GGA	GAA	TAT	TTC	ACC	CTT	CAG	ATC	CGT	GGG	CGT	GAG						
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
S	G	K	P	L	D	G	E	Y	F	T	L	Q	I	R	G	R	E						
		873				882				891				900				909					918
CGC	TTC	GAG	ATG	TTC	CGA	GAG	CTG	AAT	GAG	GCC	TTG	GAA	CTC	AAG	GAT	GCC	CAG						
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
R	F	E	M	F	R	E	L	N	E	A	L	E	L	K	D	A	Q						
		927				936				945				954				963					972
GCT	GGG	AAG	GAG	CCA	GGG	GGG	AGC	GGA	GGC	GCG	CCG	GCA	CCT	ACT	TCA	AGT	TCT						
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
A	G	K	E	P	G	G	S	G	G	A	P	A	P	T	S	S	S						
		981				990				999				1008				1017					1026
ACA	AAG	AAA	ACA	CAG	CTA	CAA	CTG	GAG	CAT	TTA	CTG	CTG	GAT	TTA	CAG	ATG	ATT						
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
T	K	K	T	Q	L	Q	L	E	H	L	L	L	D	L	Q	M	I						
		1035				1044				1053				1062				1071					1080
TTG	AAT	GGA	ATT	AAT	AAT	TAC	AAG	AAT	CCC	AAA	CTC	ACC	AGG	ATG	CTC	ACA	TTT						
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
L	N	G	I	N	N	Y	K	N	P	K	L	T	R	M	L	T	F						
		1089				1098				1107				1116				1125					1134
AAG	TTT	TAC	ATG	CCC	AAG	AAG	GCC	ACA	GAA	CTG	AAA	CAT	CTT	CAG	TGT	CTA	GAA						
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
K	F	Y	M	P	K	K	A	T	E	L	K	H	L	Q	C	L	E						
		1143				1152				1161				1170				1179					1188
GAA	GAA	CTC	AAA	CCT	CTG	GAG	GAA	GTG	CTA	AAT	TTA	GCT	CAA	AGC	AAA	AAC	TTT						
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
E	E	L	K	P	L	E	E	V	L	N	L	A	Q	S	K	N	F						
		1197				1206				1215				1224				1233					1242
CAC	TTA	AGA	CCC	AGG	GAC	TTA	ATC	AGC	AAT	ATC	AAC	GTA	ATA	GTT	CTG	GAA	CTA						
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
H	L	R	P	R	D	L	I	S	N	I	N	V	I	V	L	E	L						
		1251				1260				1269				1278				1287					1296
AAG	GGA	TCT	GAA	ACA	ACA	TTC	ATG	TGT	GAA	TAT	GCT	GAT	GAG	ACA	GCA	ACC	ATT						
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
K	G	S	E	T	T	F	M	C	E	Y	A	D	E	T	A	T	I						

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Figure 48 cont.

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		1305			1314			1323			1332			1341			1350
GTA	GAA	TTT	CTG	AAC	AGA	TGG	ATT	ACC	TTT	TGT	CAA	AGC	ATC	ATC	TCA	ACA	CTG
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
V	E	F	L	N	R	W	I	T	F	C	Q	S	I	I	S	T	L
		1359			1368			1377			Sall						
ACT	GAC	GTC	CAT	CAC	CAT	CAC	CAT	CAC	TGA	TAA	GTC	GAC					
---	---	---	---	---	---	---	---	---	---	---	---	---					
T	D	V	H	H	H	H	H	H	*	*							

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Figure 49:

5'	EcoRI		9		18		27		36		45		54					
	GAA	TTC	ACC	ATG	GGA	TGG	AGC	TGT	ATC	ATC	CTC	TTC	TTG	GTA	GCA	ACA	GCT	ACA
				M	G	W	S	C	I	I	L	F	L	V	A	T	A	T
	63		72		81		90		99		108							
	GGT	GTA	CAC	TCC	GAT	ATC	CAG	CTG	ACC	CAG	TCT	CCA	GCA	ATC	ATG	TCT	GCA	TCT
	G	V	H	S	D	I	Q	L	T	Q	S	P	A	I	M	S	A	S
	117		126		135		144		153		162							
	CCA	GGG	GAA	AAG	GTC	ACC	ATG	ACC	TGC	AGG	GCC	AGC	TCA	AGT	GTT	AGT	TCC	AGT
	P	G	E	K	V	T	M	T	C	R	A	S	S	S	V	S	S	S
	171		180		189		198		207		216							
	TAC	TTG	CAC	TGG	TAC	CAG	CAG	AAG	TCA	GGT	GCC	TCC	CCC	AAA	CTC	TGG	ATT	TAT
	Y	L	H	W	Y	Q	Q	K	S	G	A	S	P	K	L	W	I	Y
	225		234		243		252		261		270							
	AGC	ACA	TCC	AAC	TTG	GCT	TCT	GGA	GTC	CCT	GCT	CGC	TTC	AGT	GGC	AGT	GGG	TCT
	S	T	S	N	L	A	S	G	V	P	A	R	F	S	G	S	G	S
	279		288		297		306		315		324							
	GGG	ACC	TCT	TAC	TCT	CTC	ACA	ATC	AGC	AGT	GTG	GAG	GCT	GAA	GAT	GCT	GCC	ACT
	G	T	S	Y	S	L	T	I	S	S	V	E	A	E	D	A	A	T
	333		342		351		360		369		378							
	TAT	TAC	TGC	CAG	CAG	TAC	AGT	GGT	TAC	CCG	TAC	ACG	TTC	GGA	GGG	GGG	ACC	AAG
	Y	Y	C	Q	Q	Y	S	G	Y	P	Y	T	F	G	G	G	T	K
	387		396		405		414		423		432							
	CTC	GAG	ATC	AAA	GGT	GGT	GGT	GGT	TCT	GGC	GGC	GGC	GGC	TCC	GGT	GGT	GGT	GGT
	L	E	I	K	G	G	G	G	S	G	G	G	G	S	G	G	G	G
	441		450		459		468		477		486							
	TCT	CAG	GTG	AAA	CTG	CAG	GAG	TCT	GGG	GCT	GAG	CTT	GTG	AAG	CCT	GGG	GCT	TCA
	S	Q	V	K	L	Q	E	S	G	A	E	L	V	K	P	G	A	S
	495		504		513		522		531		540							
	GTG	AAG	CTG	TCC	TGC	AAG	GCT	TCT	GGC	TAC	ACC	CTC	ACC	AGC	TAC	TGG	TTG	CAC
	V	K	L	S	C	K	A	S	G	Y	T	L	T	S	Y	W	L	H
	549		558		567		576		585		594							
	TGG	GTG	AAG	CAG	TGG	CCT	GGA	CGA	GGC	CTT	GAG	TGG	ATT	GGA	AGG	ATT	GAT	CCC
	W	V	K	Q	W	P	G	R	G	L	E	W	I	G	R	I	D	P
	603		612		621		630		639		648							
	AAT	AGT	GGT	GGT	ACT	AAG	TAC	GAT	GAG	AAG	TTC	AAG	AGC	AAG	GCC	ACA	CTG	ACT
	N	S	G	G	T	K	Y	D	E	K	F	K	S	K	A	T	L	T

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Figure 49 cont.

657	666	675	684	693	702
GTA GAC AAA CCC TCC	AGC ACA GCC TAC	ATG CAG CTC AGC AGC	CTG ACA TCT	GAG	
V D K P S	S T A Y M Q	L S S L T S	E		
711	720	729	738	747	756
GAC TCT GCG GTC TAT	TAT TGT GCA AGA	TGG GAC TAC TGG GGC	CAA GGG ACC	ACG	
D S A V Y Y C A R W	D Y W G Q G T T				
765	774	783	792	801	810
GTC ACC GTC TCC TCC	GGA ACC CCG CTG	GGT GAC ACC ACC	CAC ACT AGT GGA	AAA	
V T V S S G T P L G	D T T H T S G K				
819	828	837	846	855	864
CCA CTG GAT GGA GAA	TAT TTC ACC CTT	CAG ATC CGT GGG	CGT GAG CGC TTC	GAG	
P L D G E Y F T L Q	I R G R E R F E				
873	882	891	900	909	918
ATG TTC CGA GAG CTG	AAT GAG GCC TTG	GAA CTC AAG GAT	GCC CAG GCT GGG	AAG	
M F R E L N E A L E	L K D A Q A G K				
927	936	945	954	963	972
GAG CCA GGG GGG TCC	GGA GGT GGT GGT	AGC ACC CAA GTG	TGC ACC GGC ACA	GAC	
E P G G S G G G G	S T Q V C T G T D				
981	990	999	1008	1017	1026
ATG AAG CTG CGG CTC	CCT GCC AGT CCC	GAG ACC CAC CTG	GAC ATG CTC CGC	CAC	
M K L R L P A S P	E T H L D M L R H				
1035	1044	1053	1062	1071	1080
CTC TAC CAG GGC TGC	CAG GTG GTG CAG	GGA AAC CTG GAA	CTC ACC TAC CTG	CCC	
L Y Q G C Q V V Q	G N L E L T Y L P				
1089	1098	1107	1116	1125	1134
ACC AAT GCC AGC CTG	TCC TTC CTG CAG	GAT ATC CAG GAG	GTG CAG GGC TAC	GTG	
T N A S L S F L Q	D I Q E V Q G Y V				
1143	1152	1161	1170	1179	1188
CTC ATC GCT CAC AAC	CAA GTG AGG CAG	GTC CCA CTG CAG	AGG CTG CGG ATT	GTG	
L I A H N Q V R Q	V P L Q R L R I V				
1197	1206	1215	1224	1233	1242
CGA GGC ACC CAG CTC	TTT GAG GAC AAC	TAT GCC CTG GCC	GTG CTA GAC AAT	GGA	
R G T Q L F E D N Y	A L A V L D N G				
1251	1260	1269	1278	1287	1296
GAC CCG CTG AAC AAT	ACC ACC CCT GTC	ACA GGG GCC TCC	CCA GGA GGC CTG	CGG	
D P L N N T T P V	T G A S P G G L R				

Figure 49 cont.

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1305	1314	1323	1332	1341	1350
GAG CTG CAG CTT CGA AGC CTC ACA GAG ATC TTG AAA GGA GGG GTC TTG ATC CAG					
E L Q L R S L T E I L K G G V L I Q					
1359	1368	1377	1386	1395	1404
CGG AAC CCC CAG CTC TGC TAC CAG GAC ACG ATT TTG TGG AAG GAC ATC TTC CAC					
R N P Q L C Y Q D T I L W K D I F H					
1413	1422	1431	1440	1449	1458
AAG AAC AAC CAG CTG GCT CTC ACA CTG ATA GAC ACC AAC CGC TCT CGG GCC TGC					
K N N Q L A L T L I D T N R S R A C					
1467	1476	1485	1494	1503	1512
CAC CCC TGT TCT CCG ATG TGT AAG GGC TCC CGC TGC TGG GGA GAG AGT TCT GAG					
H P C S P M C K G S R C W G E S S E					
1521	1530	1539	1548	1557	1566
GAT TGT CAG AGC CTG ACG CGC ACT GTC TGT GCC GGT GGC TGT GCC CGC TGC AAG					
D C Q S L T R T V C A G G C A R C K					
1575	1584	1593	1602	1611	1620
GGG CCA CTG CCC ACT GAC TGC TGC CAT GAG CAG TGT GCT GCC GGC TGC ACG GGC					
G P L P T D C C H E Q C A A G C T G					
1629	1638	1647	1656	1665	1674
CCC AAG CAC TCT GAC TGC CTG GCC TGC CTC CAC TTC AAC CAC AGT GGC ATC TGT					
P K H S D C L A C L H F N H S G I C					
1683	1692	1701	1710	1719	1728
GAG CTG CAC TGC CCA GCC CTG GTC ACC TAC AAC ACA GAC ACG TTT GAG TCC ATG					
E L H C P A L V T Y N T D T F E S M					
1737	1746	1755	1764	1773	1782
CCC AAT CCC GAG GGC CGG TAT ACA TTC GGC GCC AGC TGT GTG ACT GCC TGT CCC					
P N P E G R Y T F G A S C V T A C P					
1791	1800	1809	1818	1827	1836
TAC AAC TAC CTT TCT ACG GAC GTG GGA TCC TGC ACC CTC GTC TGC CCC CTG CAC					
Y N Y L S T D V G S C T L V C P L H					
1845	1854	1863	1872	1881	1890
AAC CAA GAG GTG ACA GCA GAG GAT GGA ACA CAG CGG TGT GAG AAG TGC AGC AAG					
N Q E V T A E D G T Q R C E K C S K					
1899	1908	1917	1926	1935	1944
CCC TGT GCC CGA GTG TGC TAT GGT CTG GGC ATG GAG CAC TTG CGA GAG GTG AGG					
P C A R V C Y G L G M E H L R E V R					

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Figure 49 cont.

1953			1962			1971			1980			1989			1998		
GCA	GTT	ACC	AGT	GCC	AAT	ATC	CAG	GAG	TTT	GCT	GGC	TGC	AAG	AAG	ATC	TTT	GGG
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
A	V	T	S	A	N	I	Q	E	F	A	G	C	K	K	I	F	G
2007			2016			2025			2034			2043			2052		
AGC	CTG	GCA	TTT	CTG	CCG	GAG	AGC	TTT	GAT	GGG	GAC	CCA	GCC	TCC	AAC	ACT	GCC
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
S	L	A	F	L	P	E	S	F	D	G	D	P	A	S	N	T	A
2061			2070			2079			2088			2097			2106		
CCG	CTC	CAG	CCA	GAG	CAG	CTC	CAA	GTG	TTT	GAG	ACT	CTG	GAA	GAG	ATC	ACA	GGT
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
P	L	Q	P	E	Q	L	Q	V	F	E	T	L	E	E	I	T	G
2115			2124			2133			2142			2151			2160		
TAC	CTA	TAC	ATC	TCA	GCA	TGG	CCG	GAC	AGC	CTG	CCT	GAC	CTC	AGC	GTC	TTC	CAG
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Y	L	Y	I	S	A	W	P	D	S	L	P	D	L	S	V	F	Q
2169			2178			2187			2196			2205			2214		
AAC	CTG	CAA	GTA	ATC	CGG	GGA	CGA	ATT	CTG	CAC	AAT	GGC	GCC	TAC	TCG	CTG	ACC
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
N	L	Q	V	I	R	G	R	I	L	H	N	G	A	Y	S	L	T
2223			2232			2241			2250			2259			2268		
CTG	CAA	GGG	CTG	GGC	ATC	AGC	TGG	CTG	GGG	CTG	CGC	TCA	CTG	AGG	GAA	CTG	GGC
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
L	Q	G	L	G	I	S	W	L	G	L	R	S	L	R	E	L	G
2277			2286			2295			2304			2313			2322		
AGT	GGA	CTG	GCC	CTC	ATC	CAC	CAT	AAC	ACC	CAC	CTC	TGC	TTC	GTG	CAC	ACG	GTG
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
S	G	L	A	L	I	H	H	N	T	H	L	C	F	V	H	T	V
2331			2340			2349			2358			2367			2376		
CCC	TGG	GAC	CAG	CTC	TTT	CGG	AAC	CCG	CAC	CAA	GCT	CTG	CTC	CAC	ACT	GCC	AAC
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
P	W	D	Q	L	F	R	N	P	H	Q	A	L	L	H	T	A	N
2385			2394			2403			2412			2421			2430		
CGG	CCA	GAG	GAC	GAG	TGT	GTG	GGC	GAG	GGC	CTG	GCC	TGC	CAC	CAG	CTG	TGC	GCC
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
R	P	E	D	E	C	V	G	E	G	L	A	C	H	Q	L	C	A
2439			2448			2457			2466			2475			2484		
CGA	GGG	CAC	TGC	TGG	GGT	CCA	GGG	CCC	ACC	CAG	TGT	GTC	AAC	TGC	AGC	CAG	TTC
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
R	G	H	C	W	G	P	G	P	T	Q	C	V	N	C	S	Q	F
2493			2502			2511			2520			2529			2538		
CTT	CGG	GGC	CAG	GAG	TGC	GTG	GAG	GAA	TGC	CGA	GTA	CTG	CAG	GGG	CTC	CCC	AGG
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
L	R	G	Q	E	C	V	E	E	C	R	V	L	Q	G	L	P	R
2547			2556			2565			2574			2583			2592		
GAG	TAT	GTG	AAT	GCC	AGG	CAC	TGT	TTG	CCG	TGC	CAC	CCT	GAG	TGT	CAG	CCC	CAG
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
E	Y	V	N	A	R	H	C	L	P	C	H	P	E	C	Q	P	Q

*

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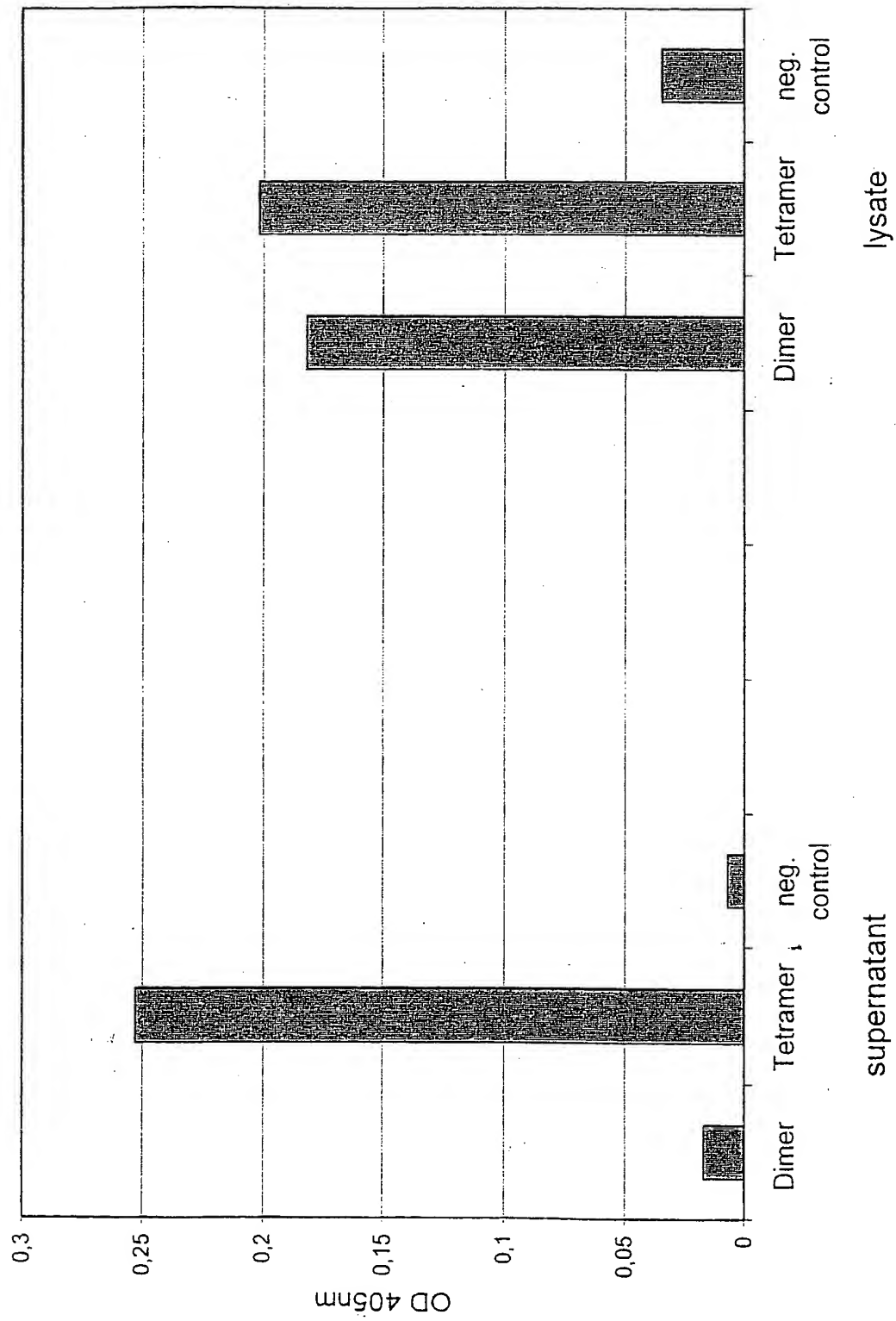
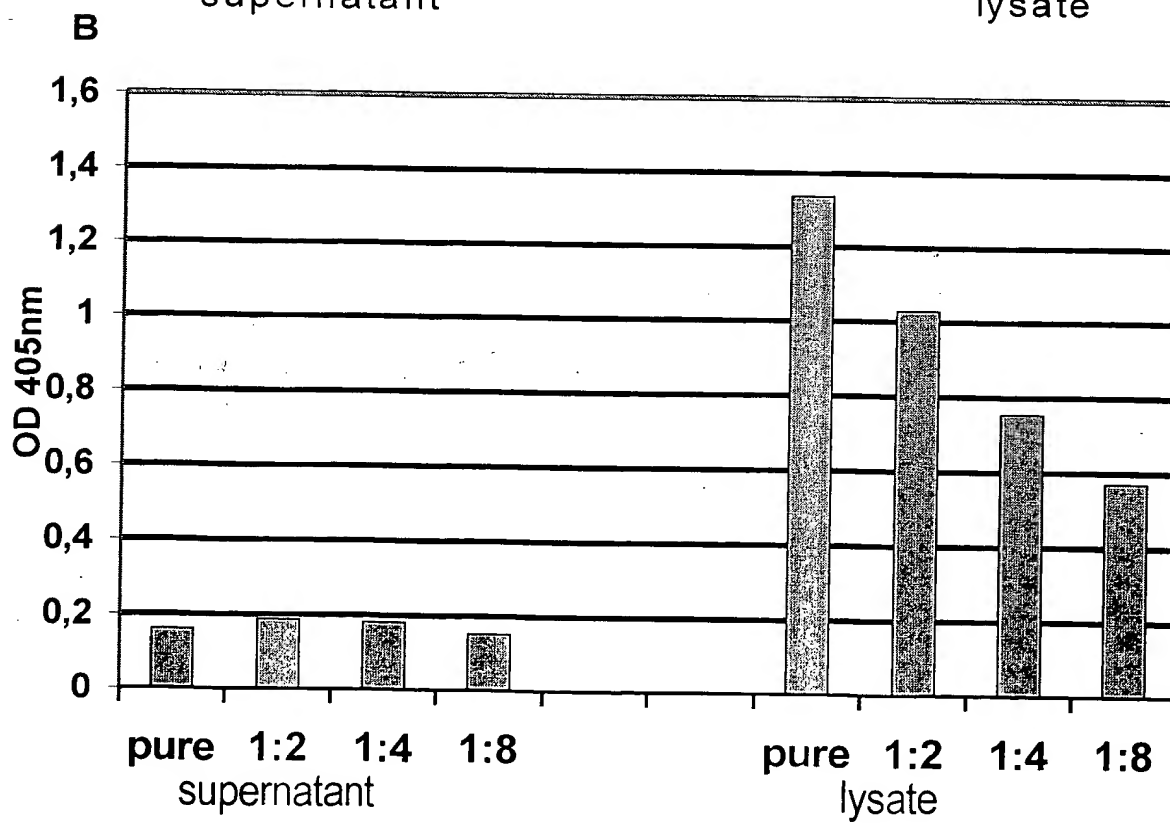
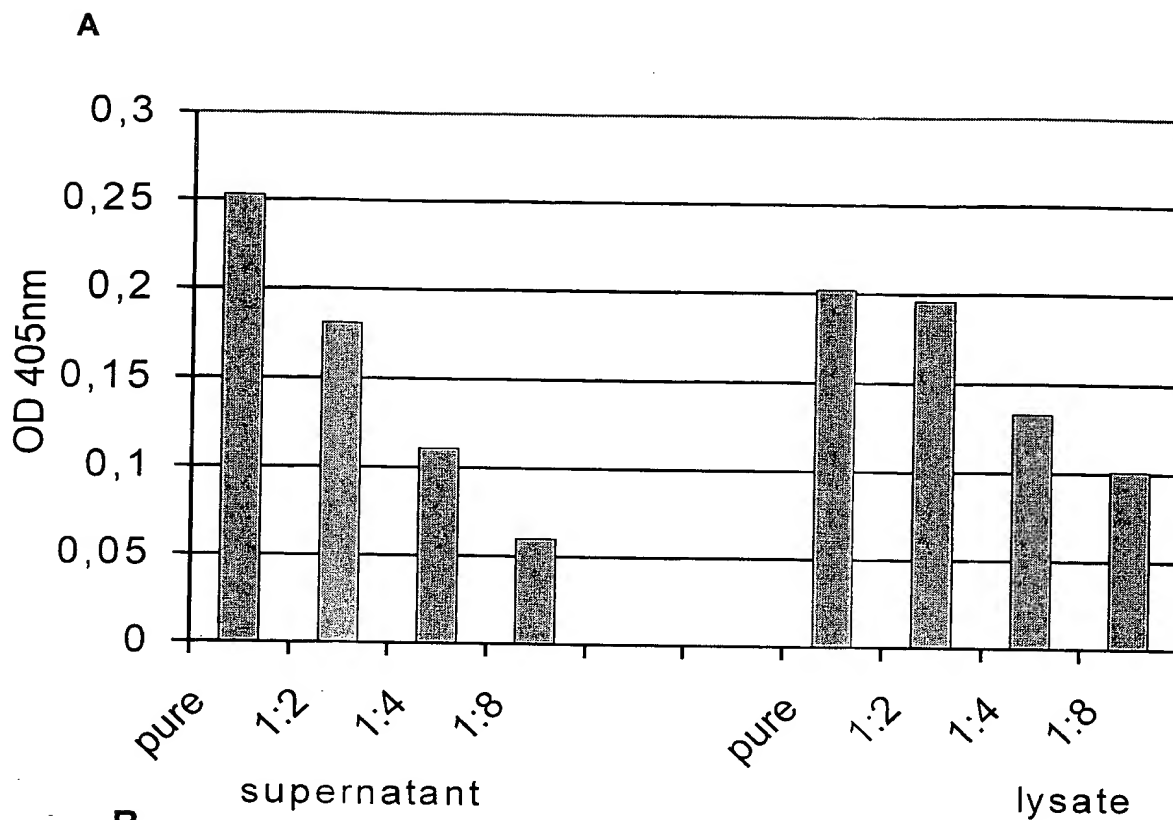


Figure 50

Figure 51

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N-Terminally Linked Effector Functions



Figure 53

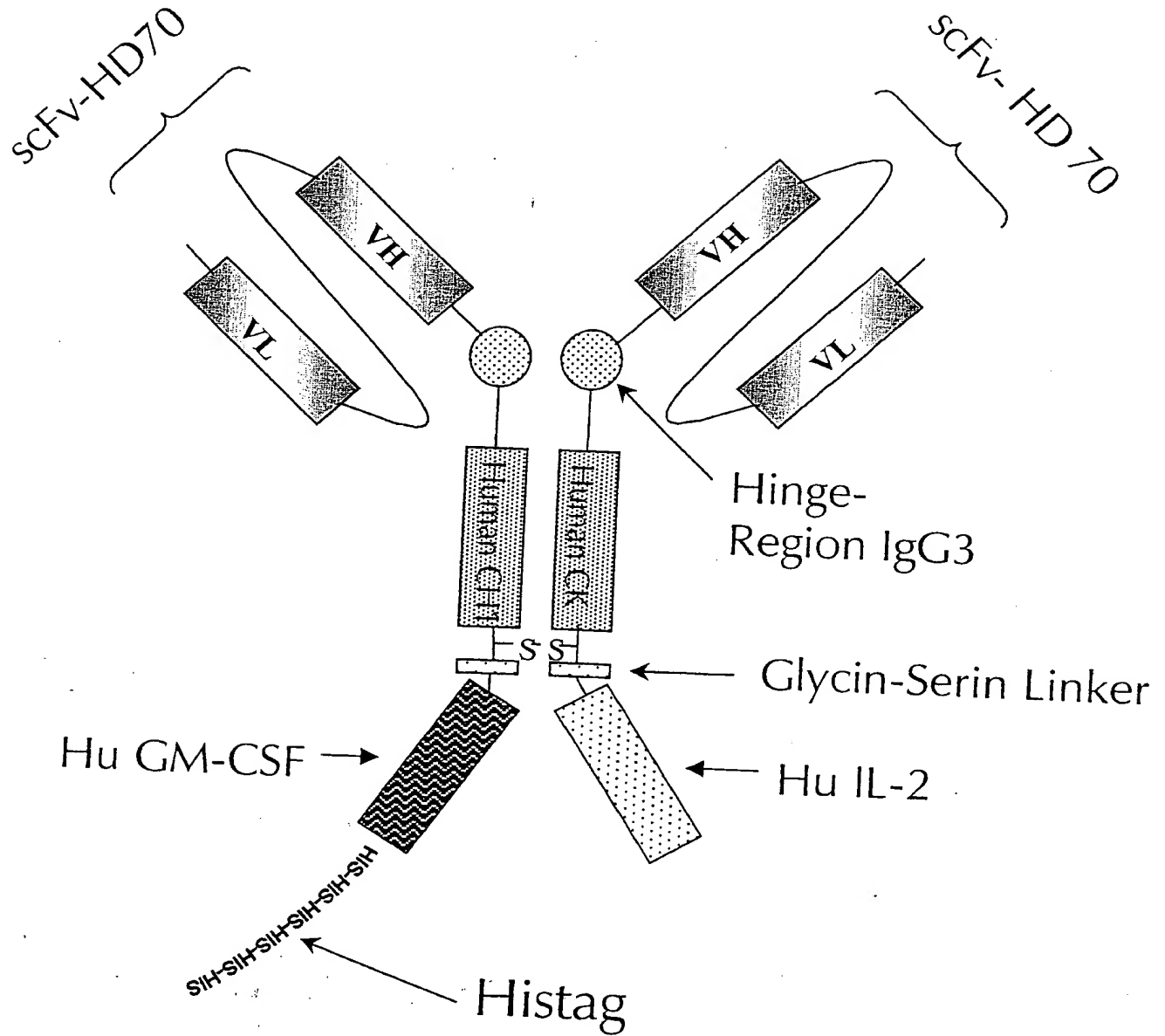


Figure 54

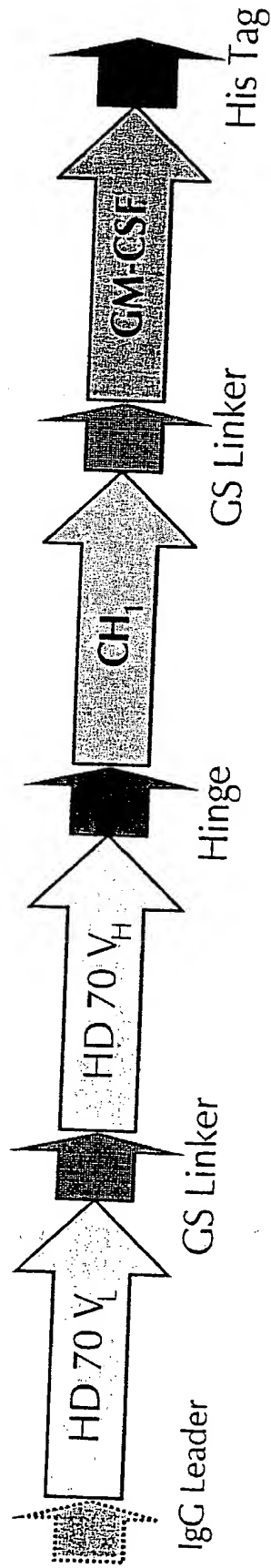
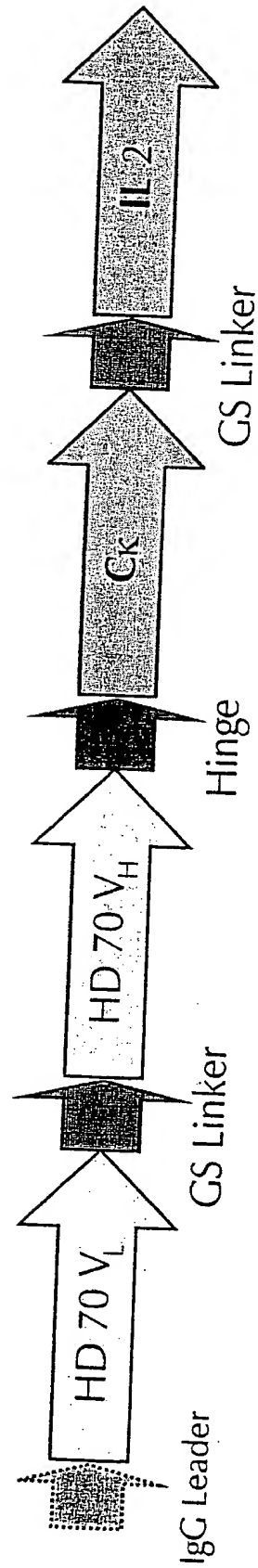
HD 70 scFv - CH1-GM-CSF:**HD 70 scFv - Cκ-IL 2:**

Figure 55a

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+3
 EcoRI M G W S C I I
 NcoI
 1 TTTTCTTCTT CCATTTCAGG TGTCGTGAGG AATTCACCAT GGGATGGAGC TGTATCATCC
 AAAAAAGAA GGTAAGTCC ACAGCACTCC TTAAGTGGTA CCCTACCTCG ACATAGTAGG

+3 L F L V A T A T G V H S E L Q M T Q S P
 BsrGI SacI
 61 TCTTCTTGGT AGCAACAGCT ACAGGTGTAC ACTCCGAGCT CCAGATGACC CAGTCTCCAT
 AGAAGAACCA TCGTTGTGCA TGTCCACATG TGAGGCTCGA GGTCTACTGG GTCAGAGGTA

+3 S S L S A S V G D R V T I T C R A S Q S
 121 CCTCCCTGTC TGCATCTGTA GGAGACAGAG TCACCATCAC TTGCCGGGCA AGTCAGAGCA
 GGAGGGACAG ACGTAGACAT CCTCTGTCTC AGTGGTAGTG AACGGCCCGT TCAGTCTCGT

+3 I S S Y L N W Y Q Q K P G Q P P K L L I
 SwaI
 181 TTAGCAGCTA TTAAATTGG TATCAGCAGA AACCAGGACA GCCTCCTAAG CTGCTCATTT
 AATCGTCGAT AAATTTAACC ATAGTCGTCT TTGGTCCTGT CGGAGGATTC GACGAGTAAA

+3 Y W A S T R E S G V P D R F S G S E S G
 SmaI
 241 ACTGGGCATC TACCCGGGAA TCCGGGGTCC CTGACCGATT CAGCGGCAGT GAATCTGGGA
 TGACCCGTAG ATGGGCCCTT AGGCCCCAGG GACTGGCTAA GTCGCCGTCA CTTAGACCTT

+3 T N Y T L T I S S L Q P E D F A T Y F C
 PstI
 301 CAAATTACAC TCTCACCATC AGCAGCCTGC AGCCTGAAGA TTTTGCTACT TACTTTTGTG
 GTTTAATGTG AGAGTGGTAG TCGTCGGACG TCGGACTTCT AAAACGATGA ATGAAAACAG

+3 Q Q S D S L P I T F G Q G T R L D I Q G
 361 AACAGTCTGA CAGTTTGCCG ATCACCTTCG GCCAAGGGAC ACGACTGGAC ATTCAAGGAG
 TTGTCACTGT GTCAAACGGC TAGTGGAAGC CGGTTCCCTG TGCTGACCTG TAAGTTCCCT

+3 G G G S G G G G S G G G G S E V Q L L E
 PvuII
 421 GAGGAGGATC AGGTGGTGGT GGTAGCGGCG GCGGCGGCTC AGAGGTGCAG CTGCTCGAGT
 CTCCTCCTAG TCCACCACCA CCATCGCCGC CGCCGCCGAG TCTCCACGTC GACGAGCTCA

+3 S G G G V V Q P G R S L R L S C A A S G
 481 CTGGGGGAGG CGTGGTCCAG CCTGGGAGGT CCCTGAGACT CTCCTGTGCA GCCTCTGGAT
 GACCCCTCC GCACCAGGTC GGACCCTCCA GGGACTCTGA GAGGACACGT CGGAGACCTA

+3 F T F S S Y G M H W V R Q A P G K G L E
 541 TCACCTTCAG TAGCTATGGC ATGCACTGGG TCCGCCAGGC TCCAGGCAAG GGGCTGGAGT
 AGTGGAAGTC ATCGATACCG TACGTGACCC AGGCGGTCCG AGGTCCGTTT CCCGACCTCA

+3 W V A V I S Y D G S N K Y Y A D S V K G
 NdeI
 601 GGGTGGCAGT TATATCATAT GATGGAAGTA ATAAATACTA TGCAGACTCC GTGAAGGGCC
 CCCACCGTCA ATATAGTATA CTACCTTCAT TATTTATGAT ACGTCTGAGG CACTTCCCGG

+3 R F T I S R D N S K N T L Y L Q M N S L
 661 GATTACCAT CTCCAGAGAC AATTCCAAGA ACACGCTGTA TCTGCAAATG AACAGCCTGA
 CTAAGTGGTA GAGGTCTCTG TTAAGGTTCT TGTGCGACAT AGACGTTTAC TTGTCGGACT

+3 R A E D T A V Y Y C A K D M G W G S G W
 721 GAGCTGAGGA CACGGCTGTG TATTACTGTG CGAAAGATAT GGGGTGGGGC AGTGGCTGGA
 CTCGACTCCT GTGCCGACAC ATAATGACAC GCTTTCTATA CCCCACCCCG TCACCGACCT

Figure 55a cont.

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+3 R P Y Y Y Y G M D V W G Q G T T V T V S
BspEI

781 GACCCTACTA CTACTACGGT ATGGACGTCT GGGGCCAAGG GACCACGGTC ACCGTCTCCT
CTGGGATGAT GATGATGCCA TACCTGCAGA CCCCGGTTCC CTGGTGCCAG TGGCAGAGGA

+3 S G T P L G D T T H T A S T K G P S V F
BspEI NheI

841 CCGGAACCCC GCTGGGTGAC ACCACCCACA CCGCTAGCAC CAAGGGCCCA TCGGTCTTCC
GGCCTTGGGG CGACCCACTG TGGTGGGTGT GGCATCGTG GTTCCCGGT AGCCAGAAGG

+3 P L A P S S K S T S G G T A A L G C L V
901 CCCTGGCACC CTCCTCCAAG AGCACCTCTG GGGGCACAGC GGCCCTGGGC TGCCTGGTCA
GGGACCGTGG GAGGAGGTTT TCGTGGAGAC CCCCGTGTGC CCGGACCCG ACGGACCACT

+3 K D Y F P E P V T V S W N S G A L T S G
AgeI

961 AGGACTACTT CCCGAACCG GTGACGGTGT CGTGGAATC AGGCGCCCTG ACCAGCGGCG
TCCTGATGAA GGGGCTTGGC CACTGCCACA GCACCTTGAG TCCGCGGGAC TGGTCGCCCG

+3 V H T F P A V L Q S S G L Y S L S S V V
1021 TGCACACCTT CCCGGCTGTC CTACAGTCTT CAGGACTCTA CTCCCTCAGC AGCGTGGTGA
ACGTGTGGAA GGGCCGACAG GATGTCAGGA GTCCTGAGAT GAGGGAGTCG TCGCACCCT

+3 T V P S S S L G T Q T Y I C N V N H K P
1081 CCGTGCCCTC CAGCAGCTTG GGCACCCAGA CCTACATCTG CAACGTGAAT CACAAGCCCA
GGCACGGGAG GTCGTGAAC CCGTGGGTCT GGATGTAGAC GTTGCACTTA GTGTTCCGGT

+3 S N T K V D K K V E P K S C D K T S G G
SpeI

1141 GCAACACCAA GGTGGACAAG AAAGTTGAGC CCAAATCTTG TGACAAAAC AGTGGAGGCG
CGTTGTGGTT CCACCTGTTC TTTCAACTCG GGTTTAGAAC ACTGTTTTGA TCACCTCCCG

+3 G G S A P A R S P S P S T Q P W E H V N
1201 GTGGGTCCGC ACCCGCCCGC TCGCCAGCC CCAGCAGCA GCCCTGGGAG CATGTGAATG
CAGCCAGGCG TGGGCGGGCG AGCGGGTCGG GGTGTCGCT CGGACCCCTC GTACACTTAC

+3 A I Q E A R R L L N L S R D T A A E M N
1261 CCATCCAGGA GGCCCGCGT CTCCTGAACC TGAGTAGAGA CACTGCTGCT GAGATGAATG
GGTAGTCTT CCGGCGCGCA GAGGACTTGG ACTCATCTCT GTGACGACGA CTCTACTTAC

+3 E T V E V I S E M F D L Q E P T C L Q T
1321 AAACAGTAGA AGTCATCTCA GAAATGTTT ACCTCCAGGA GCCGACCTGC CTACAGACCC
TTTGTCTCT TCACTAGAGT CTTTACAAAC TGGAGTCTT CGGCTGGACG GATGTCTGGG

+3 R L E L Y K Q G L R G S L T K L K G P L
BsrGI

1381 GCCTGGAGCT GTACAAGCAG GGCCTGCGGG GCAGCCTCAC CAAGCTCAAG GGCCCTTGA
CGGACCTCGA CATGTTCTG CCGGACGCCC CGTCGGAGTG GTTCGAGTTC CCGGGGAAC

+3 T M M A S H Y K Q H C P P T P E T S C A
1441 CCATGATGGC CAGCCACTAC AAGCAGCACT GCCCTCCAAC CCCGAAACT TCCTGTGCAA
GGTACTACCG GTCGGTGATG TTCGTCGTGA CCGGAGGTTG GGGCCTTGA AGGACACGTT

+3 T Q I I T F E S F K E N L K D F L L V I
1501 CCCAGATTAT CACCTTTGAA AGTTTCAAAG AGAACCTGAA GGACTTTCTG CTTGTCTATC
GGGTCTAATA GTGGAACTT TCAAAGTTT TCTTGACTT CCGAAAGAC GAACAGTAGG

Figure 55a cont.

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+3 P F D C W E P V Q E H H H H. H H *

SalI

1561 CCTTTGACTG CTGGGAGCCA GTCCAGGAGC ATCATCACCA TCATCATTGA ~~~~~
GGAAACTGAC GACCCTCGGT CAGGTCTCTCG TAGTAGTGGT AGTAGTAACT GTCGACTTAA
CAGCTGAATT

1621 AACAGCTCTG
TTGTCGAGAC

+3 Figure 55b

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M' G W S C I I
EcoRI NcoI

1 TTTTCTTCTT CCATTTCAAGG TGTCGTGAGG AATTCACCAT GGGATGGAGC TGTATCATCC
 AAAAAAGAA GGTAAGTCC ACAGCACTCC TTAAGTGGTA CCCTACCTCG ACATAGTAGG

+3 L F L V A T A T G V H S E L Q M T Q S P
 BsrGI SacI

61 TCTTCTTGGT AGCAACAGCT ACAGGTGTAC ACTCCGAGCT CCAGATGACC CAGTCTCCAT
 AGAAGAACCA TCGTTGTGCA TGCCACATG TGAGGCTCGA GGTCTACTGG GTCAGAGGTA

+3 S S L S A S V G D R V T I T C R A S Q S
 121 CCTCCCTGTC TGCATCTGTA GGAGACAGAG TCACCATCAC TTGCCGGGCA AGTCAGAGCA
 GGAGGGACAG ACGTAGACAT CCTCTGTCTC AGTGGTAGTG AACGGCCCGT TCAGTCTCGT

+3 I S S Y L N W Y Q Q K P G Q P P K L L I
 SmaI

181 TTAGCAGCTA TTTAAATTGG TATCAGCAGA AACCAGGACA GCCTCCTAAG CTGCTCATTT
 AATCGTCGAT AAATTTAACC ATAGTCGTCT TTGGTCCTGT CGGAGGATTG GACGAGTAA

+3 Y W A S T R E S G V P D R F S G S E S G
 SmaI

241 ACTGGGCATC TACCCGGGAA TCCGGGGTCC CTGACCGATT CAGCGGCAGT GAATCTGGGA
 TGACCCGTAG ATGGGCCCTT AGGCCCCAGG GACTGGCTAA GTCGCCGTCA CTTAGACCCT

+3 T N Y T L T I S S L Q P E D F A T Y F C
 PstI

301 CAAATTACAC TCTCACCATC AGCAGCCTGC AGCCTGAAGA TTTTGCTACT TACTTTTGTC
 GTTTAATGTG AGAGTGGTAG TCGTCGGACG TCGGACTTCT AAAACGATGA ATGAAAACAG

+3 Q Q S D S L P I T F G Q G T R L D I Q G
 361 AACAGTCTGA CAGTTTGCCG ATCACCTTCG GCCAAGGGAC ACGACTGGAC ATTCAAGGAG
 TTGTCAGACT GTCAAACGGC TAGTGGAAGC CGGTTCCCTG TGCTGACCTG TAAGTTCTCTC

+3 G G G S G G G G S G G S E V Q L L E
 PvuII

421 GAGGAGGATC AGGTGGTGGT GGTAGCGGCG GCGGCGGCTC AGAGGTGCAG CTGCTCGAGT
 CTCCTCCTAG TCCACCACCA CCATCGCCGC CGCCGCCGAG TCTCCACGTC GACGAGCTCA

+3 S G G G V V Q P G R S L R L S C A A S G
 481 CTGGGGGAGG CGTGGTCCAG CCTGGGAGGT CCCTGAGACT CTCCTGTGCA GCCTCTGGAT
 GACCCCTCC GCACCAGGTC GGACCTCCA GGGACTCTGA GAGGACACGT CGGAGACCTA

+3 F T F S S Y G M H W V R Q A P G K G L E
 541 TCACCTCAG TAGCTATGGC ATGCACTGGG TCCGCCAGGC TCCAGGCAAG GGGCTGGAGT
 AGTGGAAGTC ATCGATACCG TACGTGACCC AGGCGGTCCG AGGTCCGTTC CCCGACCTCA

+3 W V A V I S Y D G S N K Y Y A D S V K G
 NdeI

601 GGGTGGCAGT TATATCATAT GATGGAAGTA ATAAATACTA TGCAGACTCC GTGAAGGGCC
 CCCACCGTCA ATATAGTATA CTACCTTCAT TATTTATGAT ACGTCTGAGG CACTTCCCCG

+3 R F T I S R D N S K N T L Y L Q M N S L
 661 GATTCACCAT CTCCAGAGAC AATTCCAAGA ACACGCTGTA TCTGCAAATG AACAGCCTGA
 CTAAGTGGTA GAGGTCTCTG TTAAGGTTCT TGTGCGACAT AGACGTTTAC TTGTCGGACT

+3 R A E D T A V Y Y C A K D M G W G S G W
 721 GAGCTGAGGA CACGGCTGTG TATTACTGTG CGAAAGATAT GGGGTGGGGC AGTGGCTGGA
 CTCGACTCCT GTGCCGACAC ATAATGACAC GCTTTCTATA CCCACCCCG TCACCGACCT

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Figure 55b cont.

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+3 R P Y Y Y Y G M D V W G Q G T T V T V S
BspEI

781 GACCCTACTA CTACTACGGT ATGGACGTCT GGGGCCAAGG GACCACGGTC ACCGTCTCCT
CTGGGATGAT GATGATGCCA TACCTGCAGA CCCCGGTTCC CTGGTGCCAG TGGCAGAGGA

+3 S G T P L G D T T H T R T V A A P S V F
BspEI BsiWI

841 CCGGAACCCC GCTGGGTGAC ACCACCCACA CCCGTACGGT GGCTGCACCA TCTGTCTTCA
GGCCTTGGGG CGACCCACTG TGGTGGGTGT GGGCATGCCA CCGACGTGGT AGACAGAAGT

+3 I F P P S D E Q L K S G T A S V V C L L
901 TCTTCCC GCC ATCTGATGAG CAGTTGAAAT CTGGAAGTGC CTCTGTTGTG TGCCTGCTGA
AGAAGGGCGG TAGACTACTC GTCAACTTTA GACCTTGACG GAGACAACAC ACGGACGACT

+3 N N F Y P R E A K V Q W K V D N A L Q S
961 ATAATTCTA TCCCAGAGAG GCCAAAGTAC AGTGGAAGGT GGATAACGCC CTCCAATCGG
TATTGAAGAT AGGGTCTCTC CGGTTTCATG TCACCTTCCA CCTATTGCGG GAGGTTAGCC

+3 G N S Q E S V T E Q D S K D S T Y S L S
1021 GTAATTCCCA GGAGAGTGTC ACAGAGCAGG ACAGCAAGGA CAGCACCTAC AGCCTCAGCA
CATTGAGGGT CCTCTCACAG TGTCTCGTCC TGTCGTTTCTT GTCGTGGATG TCGGAGTCGT

+3 S T L T L S K A D Y E K H K V Y A C E V
1081 GCACCCTGAC GCTGAGCAAA GCAGACTACG AGAAACACAA AGTCTACGCC TGCGAAGTCA
CGTGGGACTG CGACTCGTTT CGTCTGATGC TCTTTGTGTT TCAGATGCGG ACGCTTCAGT

+3 T H Q G L S S P V T K S F N R G E C S G
SacI

1141 CCCATCAGGG CCTGAGCTCG CCCGTCACAA AGAGCTTCAA CAGGGGAGAG TGTTCAAGGAG
GGGTAGTCCC GGACTCGAGC GGGCAGTGTT TCTCGAAGTT GTCCCCTCTC ACAAGTCCTC

+3 G G G S A P T S S S T K K T Q L Q L E H
1201 GCGGTGGGTC TGCACCTACT TCAAGTTCTA CAAAGAAAAC ACAGCTACAA CTGGAGCATT
CGCCACCCAG ACGTGGATGA AGTTCAAGAT GTTCTTTTGT TGTCGATGTT GACCTCGTAA

+3 L L L D L Q M I L N G I N N Y K N P K L
1261 TACTGCTGGA TTTACAGATG ATTTTGAATG GAATTAATAA TTACAAGAAT CCCAAACTCA
ATGACGACCT AAATGTCTAC TAAACTTAC CTTAATTATT AATGTTCTTA GGGTTTGAGT

+3 T R M L T F K F Y M P K K A T E L K H L
1321 CCAGGATGCT CACATTTAAG TTTTACATGC CCAAGAAGGC CACAGAAGTGC AAACATCTTC
GGTCCTACGA GTGTAAATTC AAAATGTACG GGTCTTCCG GTGTCTTGAC TTTGTAGAAG

+3 Q C L E E E L K P L E E V L N L A Q S K
XbaI

1381 AGTGTCTAGA AGAAGAACTC AAACCTCTGG AGGAAGTGCT AAATTTAGCT CAAAGCAAAA
TCACAGATCT TCTTCTTGAG TTTGGAGACC TCCTTCACGA TTAAATCGA GTTTCGTTTT

+3 N F H L R P R D L I S N I N V I V L E L
1441 ACTTTCATT AAGACCCAGG GACTTAATCA GCAATATCAA CGTAATAGTT CTGGAAGTAA
TGAAAGTGAA TTCTGGGTCC CTGAATTAGT CGTTATAGTT GCATTATCAA GACCTTGATT

+3 K G S E T T F M C E Y A D E T A T I V E
1501 AGGGATCTGA AACACATTC ATGTGTGAAT ATGCTGATGA GACAGCAACC ATTGTAGAAT
TCCCTAGACT TTGTTGTAAG TACACACTTA TACGACTACT CTGTCGTTGG TAACATCTTA

+3 F L N R W I T F C Q S I I S T L T * *
SalI

1561 TTCTGAACAG ATGGATTACC TTTTGTCAAA GCATCATCTC AACACTAACT TGATAAGTCG
AAGACTTGTC TACCTAATGG AAAACAGTTT CGTAGTAGAG TTGTGATTGA ACTATTACAG

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Figure 55b cont.

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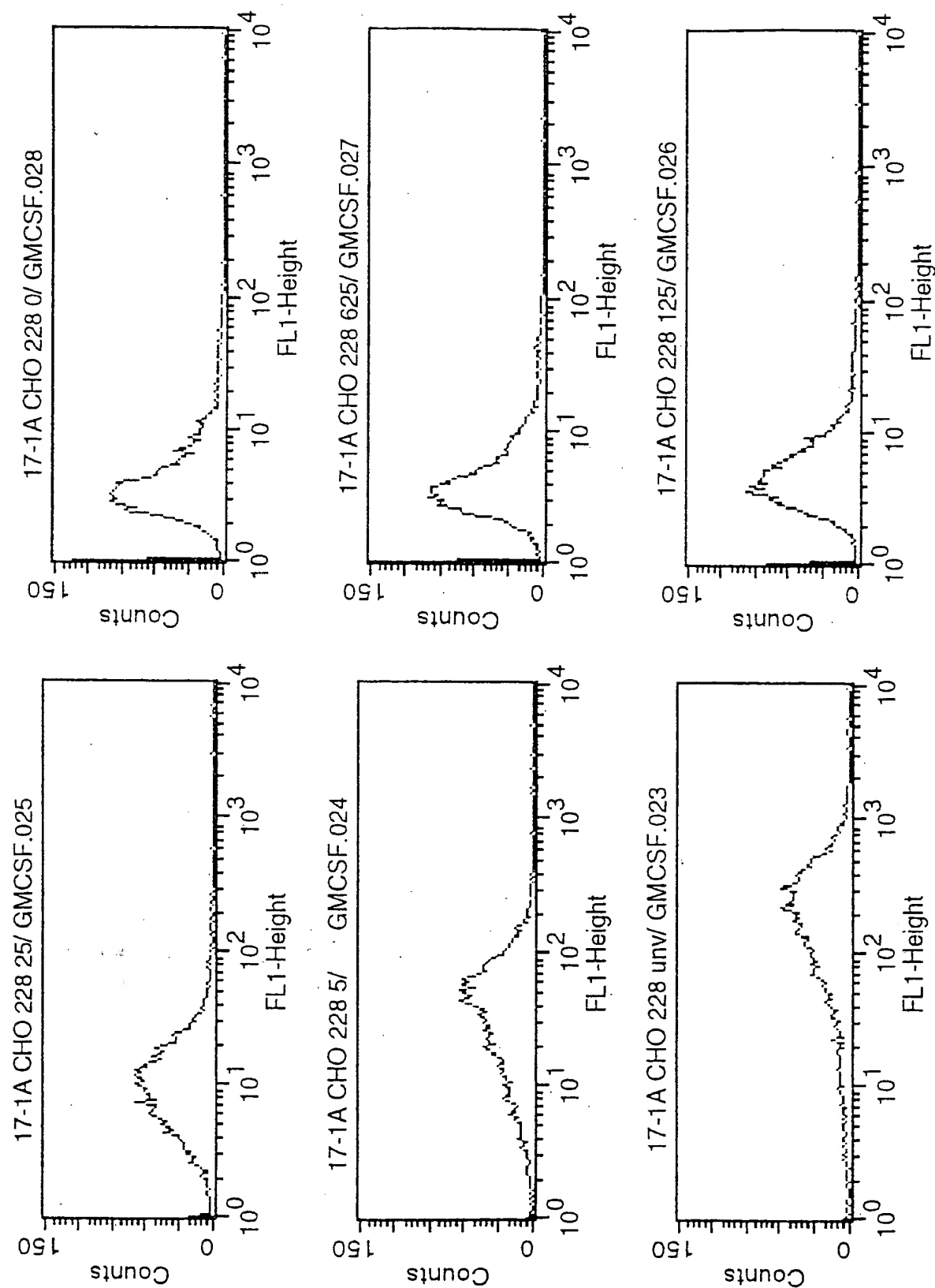
SalI

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1621 ACTTAAAACA
TGAATTTTGT

00744625 074504

Association of EpCAM Binding and GM-CSF in Heterominibody

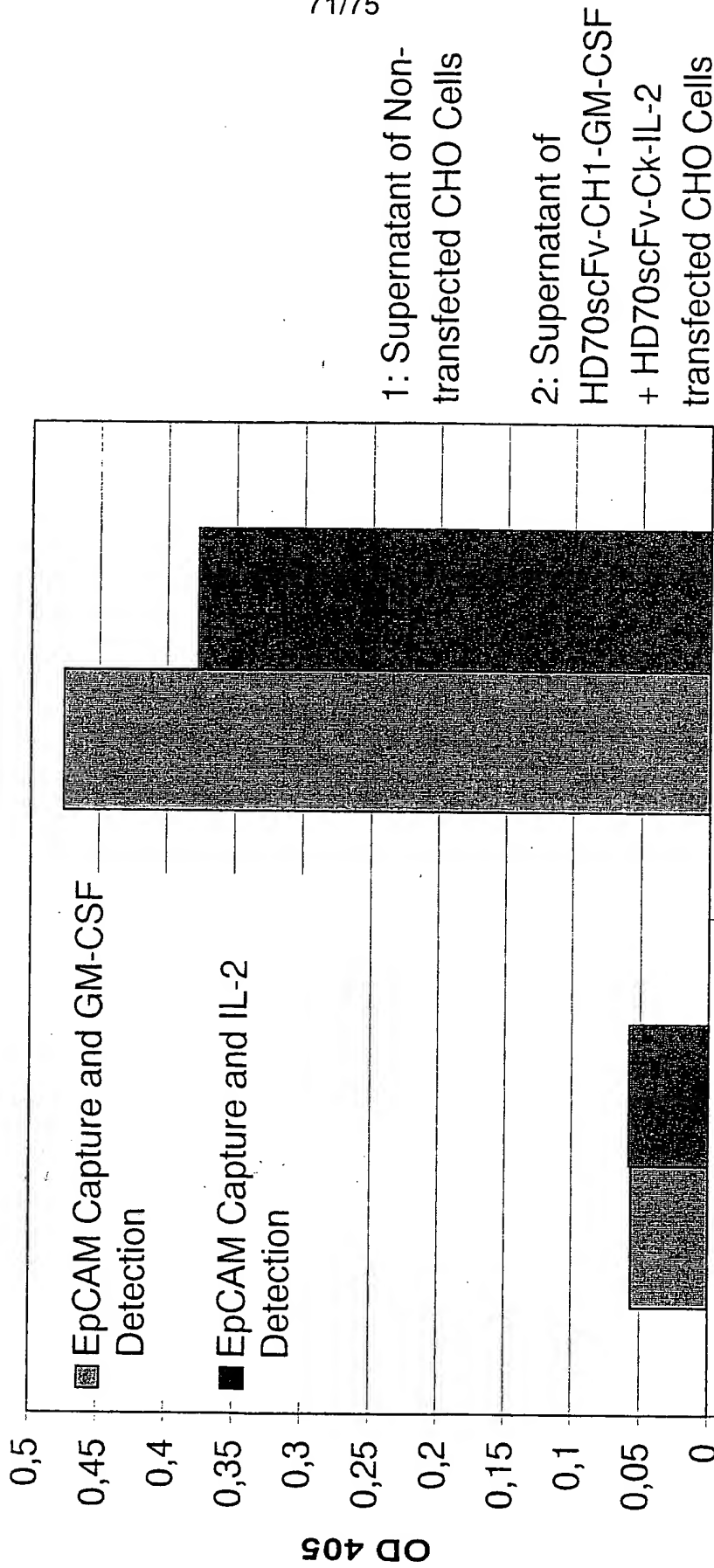


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Figure 57

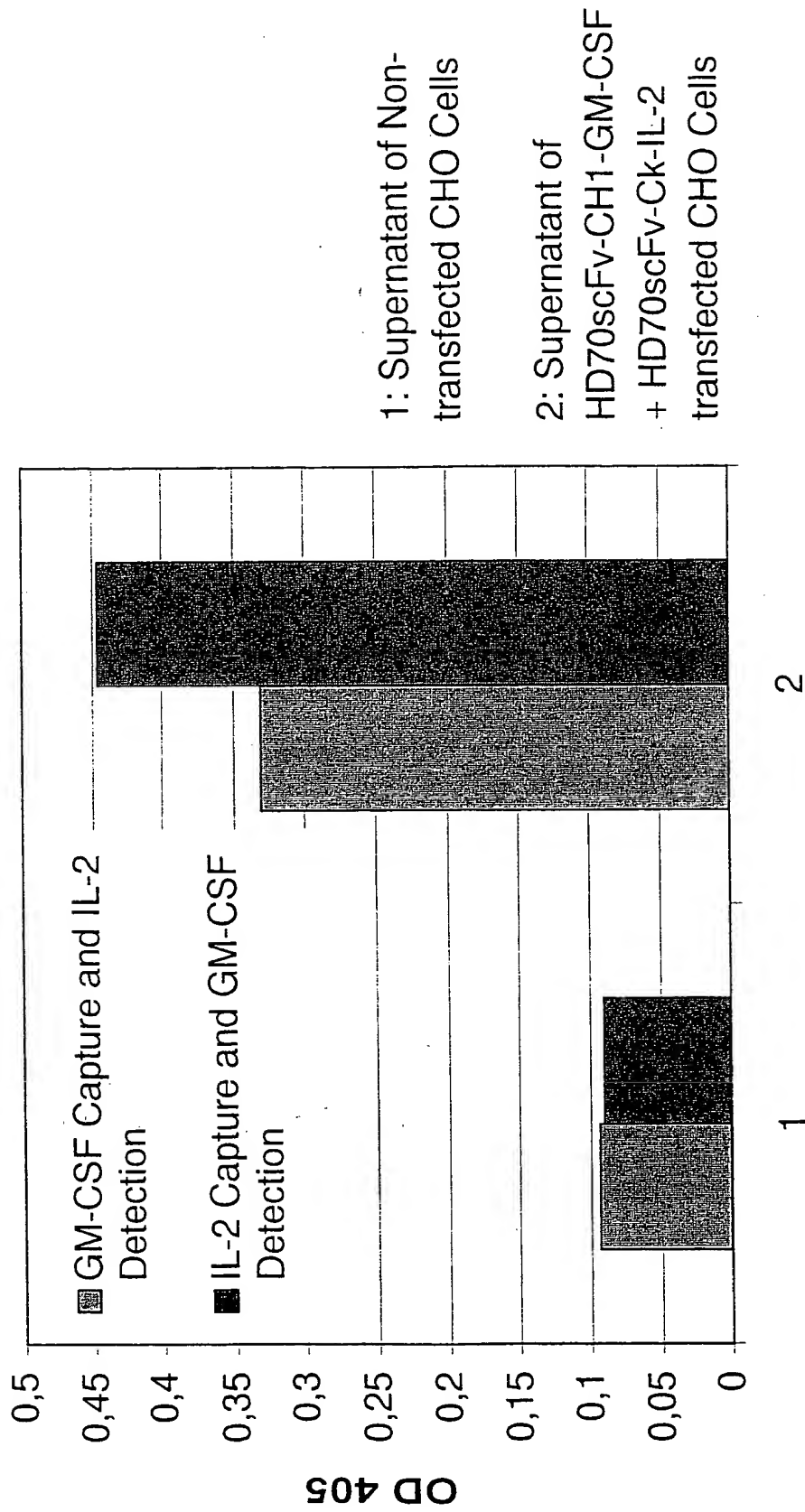
Physical Linkage of Anti-EpCAM Activity with IL-2 and GM-CSF



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Figure 58

Physical Linkage of IL-2 with GM-CSF in Heterominibody



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Figure 59

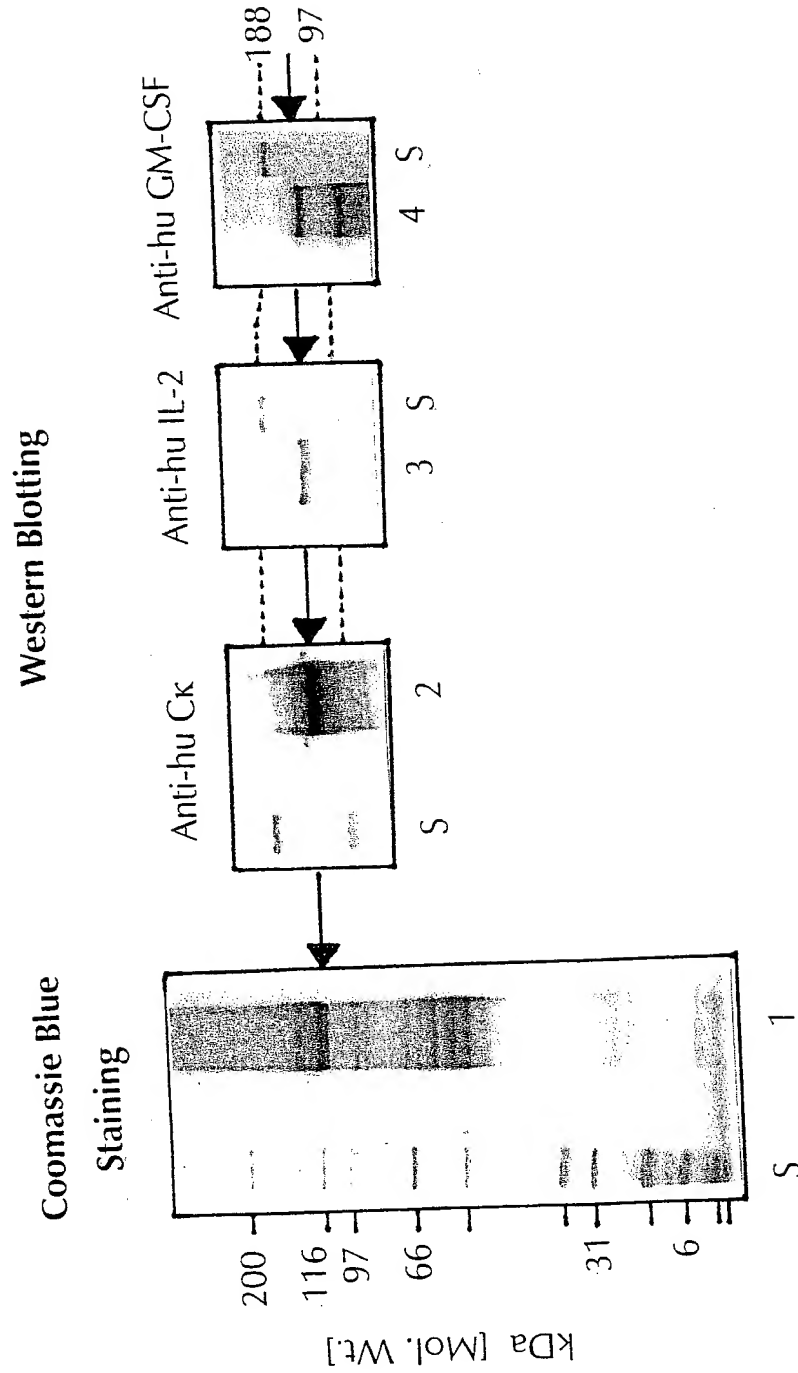
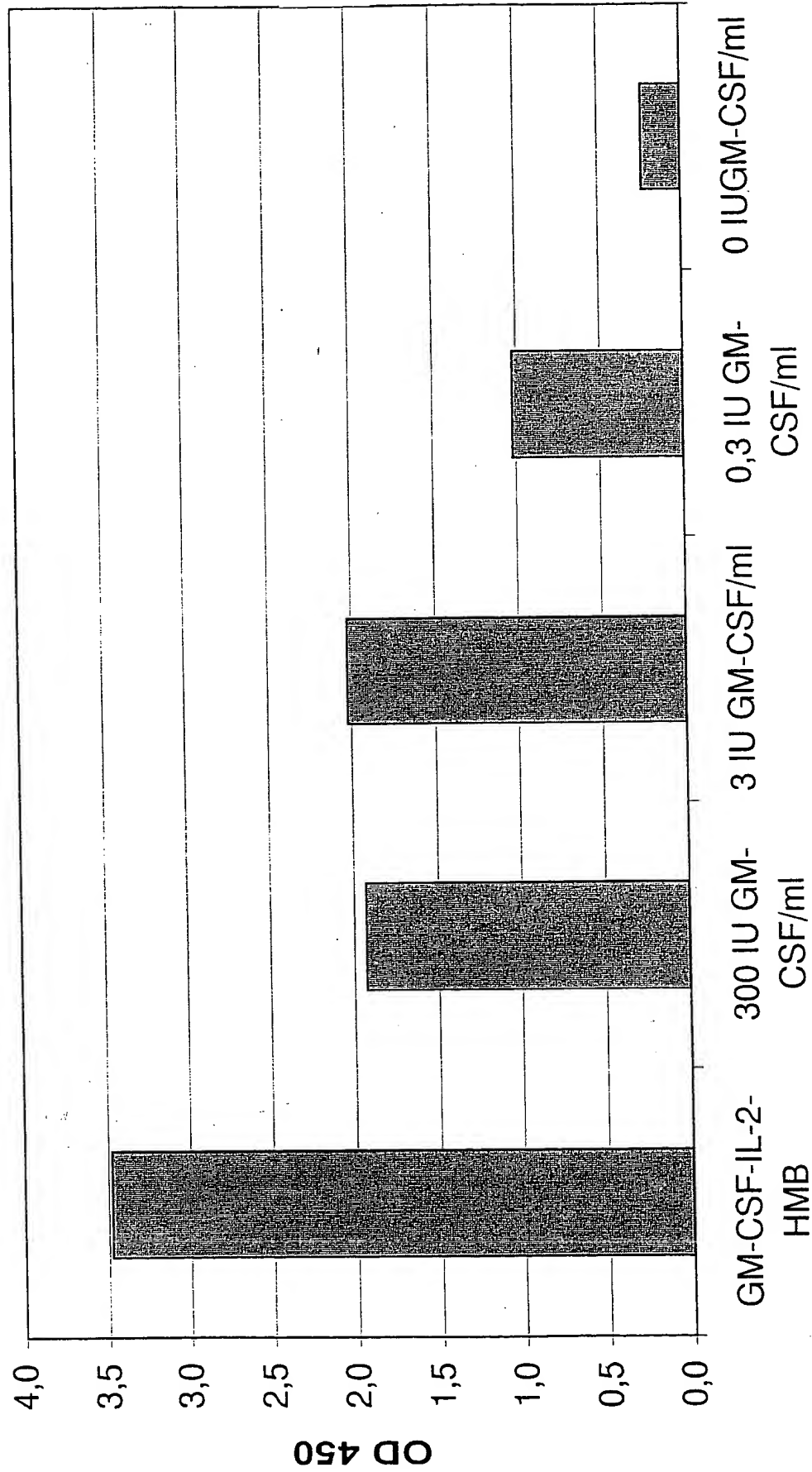


Figure 60

Bioactivity of GM-CSF in Heterominibody Format



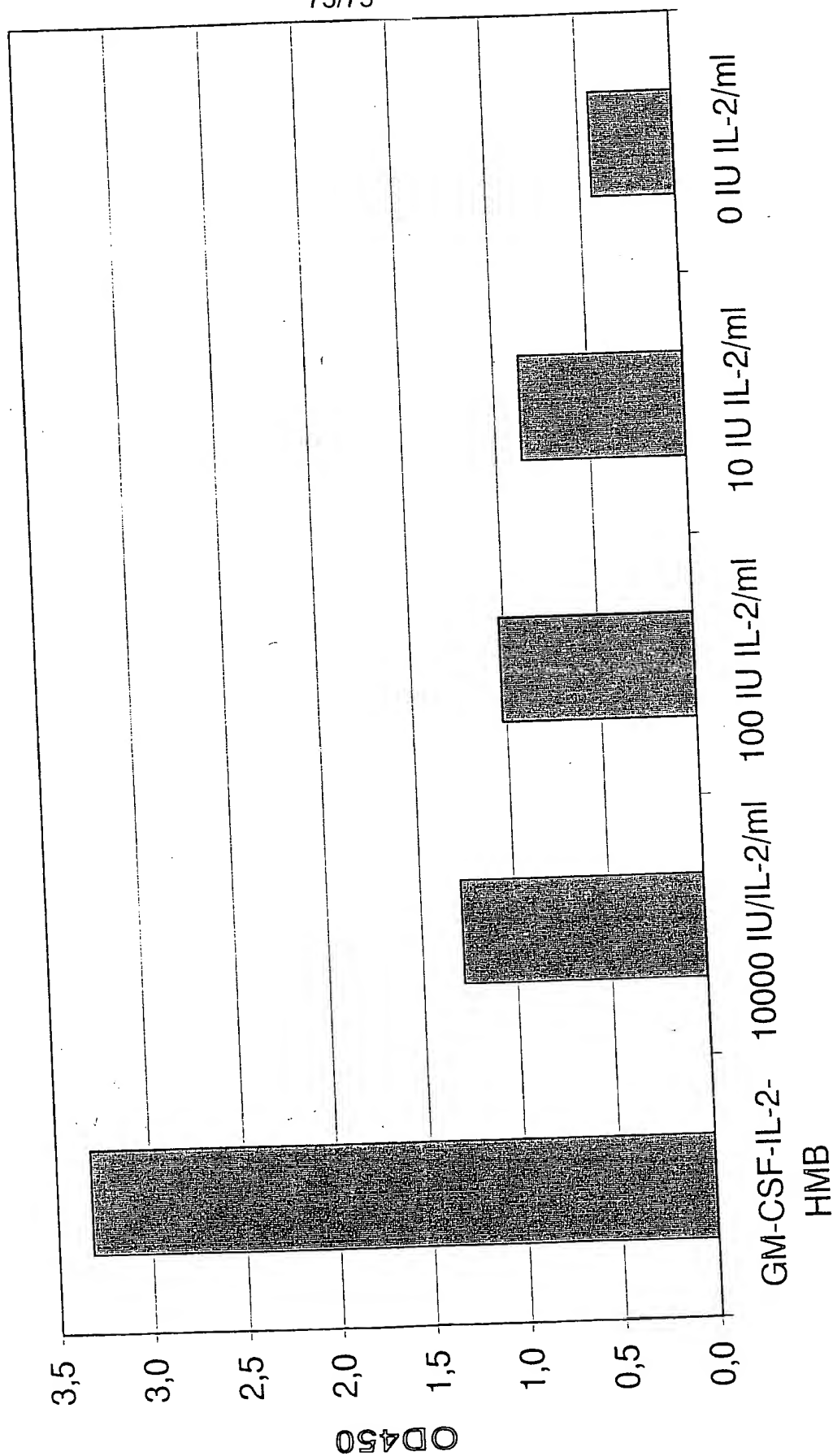
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103420 52344200

Bioactivity of IL-2 in Heteroninibody Format

Figure 61



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